COMPREHENSIVE ANALYSIS OF 20 CASES OF SYSTEMIC SCLEROSIS

Dissertation Submitted in partial
fulfillment of the university regulations for

MD DEGREE IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

(BRANCH XII A)

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CHENNAI – TAMIL NADU

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled **'COMPREHENSIVE ANALYSIS OF 20 CASES OF SYSTEMIC SCLEROSIS'** submitted by **Dr. ANBUMALAR M.** to The Tamil Nadu Dr.M.G.R. Medical University, Chennai is in partial fulfilment of the requirement for the award of M.D. [DERMATO VENEREO LEPROLOGY] and is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I, **Dr. ANBUMALAR M.** solemnly declare that the dissertation titled '**COMPREHENSIVE ANALYSIS OF 20 CASES OF SYSTEMIC SCLEROSIS'** is a bonafide work done by me at Government Rajaji Hospital during 2012 – 2014 under the guidance and supervision of **Prof. Dr. G.GEETHARANI M.D., DNB.,** Professor and Head of the Department of Dermatology, Madurai Medical College, Madurai.

I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree and diploma to any university, board either in India or abroad.

The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree in Dermatology, Venereology and Leprology (BRANCH –XII A).**

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CONTENTS

COMPREHENSIVE ANALYSIS OF 20 CASES OF SYSTEMIC SCLEROSIS

Aim - To study the epidemiological features, occupational risk factors and skin and systemic manifestations of Systemic sclerosis.

Methods – 20 Patients who presented to the outpatient department fulfilling ARA criteria for Systemic sclerosis were enrolled. A detailed history and thorough examination was done. Investigations including complete blood count, ESR, renal function tests, blood sugar, liver function tests, urine routine, X-ray chest PA view, HRCT – chest, Pulmonary function test, ultrasound of abdomen and pelvis, ECG, ECHO cardiogram, Barium Swallow, upper GI scopy, X ray of both hands were done for all the cases.

Results – Female to male ratio was 5.7:1. 95% of cases were in the age group 21 -60 years. Occupational exposure to silica, solvents, pesticides and firework were present in 11 cases. Skin tightness (100%), Raynaud's phenomenon (65%), stellate scars (90%), Round finger pad sign (85%), gangrene (10%),nek sign (80%), salt and pepper pigmentation (95%), generalized hyperpigmentation (45%), nail changes (70%) were noted. One case of mixed connective tissue disease and one case with overlap of Epidermolysis Bullosa Acquisita were recorded.

Systemic involvement, gastroesophageal reflux (85%), Interstitial lung disease (95%), pulmonary arterial hypertension (5%), acral osteolysis (75%) was present.

Conclusion – Female preponderance was noted. Occupational exposure was present in more than half of the patients. Even though skin involvement was present in all cases, 20% of cases presented only after systemic involvement. All the patients had diffuse involvement of skin. Only 65% patients had Raynaud's phenomenon, this is probably because of higher temperature present throughout the year in South India. Systemic involvement was seen in most cases, mainly involving the pulmonary, gastrointestinal system. Interstitial lung disease was present in 95% cases. No patient had renal involvement.

INTRODUCTION

Systemic sclerosis is a rare multisystem connective tissue disorder affecting the skin and internal organs. It is characterized by connective tissue sclerosis, atrophy, vascular abnormalities and autoantibodies. Female preponderance is present with peak age of onset in fourth decade.

Systemic involvement includes interstitial lung disease, pulmonary arterial hypertension, cardiac involvement, dysphagia, gastroesophageal reflux, gastrointestinal involvement, renal failure, malignant hypertension, muscle weakness, joint pain, bone involvement, calcinosis.

Diagnosis is made clinically and investigations are carried out to evaluate the systemic involvement, its extent and monitoring. It is broadly classified into two groups; limited and diffuse cutaneous systemic sclerosis based on the extent of skin involvement and systemic associations. Systemic sclerosis may be associated with other connective tissue disorders like Systemic Lupus Erythematosus, Dermatomyositis, Sjogren's syndrome, Rheumatoid arthriris, polyarthritis. Treatment includes systemic steroids, cyclophosphomide, vasodilators and treatment of specific systemic involvement.

REVIEW OF LITERATURE

SYNONYMS

Progressive Systemic Sclerosis

Systemic Scleroderma

Acrosclerosis

LITERAL MEANING

The word "scleroderma" has its origin from Greek; "sclero" means hard and "derma" means skin. The term Progressive systemic sclerosis is better avoided because of variable course of the disease.

HISTORICAL ASPECTS

Hippocrates was first to describe this condition as thickened skin[1]. Scleroderma was then described in 1753 in a 17-year-old woman from Naples by Carlo Curzio[1]. In 1847 the term 'Sclerodermie' was coined by Gintrac[2]. A.J. Maurice Raynaud described Raynaud's phenomenon in 1862, and in 1871 he described its association with Systemic sclerosis[3]. Sir William Osler [4] gave the most vivid description of disease in 1898 - "In its more aggravated forms diffuse scleroderma is one of the most terrible of all human ills. Like Tithoneus to 'wither slowly', and like him to be beaten down and marred and wasted until one is literally a mummy,

encased in an ever shrinking, slowly contracting skin of steel, is a fate not pictured in any tragedy, ancient or modern" . It was in 1945 visceral involvement became an accepted complication and the term Progressive Systemic sclerosis was coined by Goetz[1]. Later the word progressive was omitted as the disease has a variable course. Matsui described the typical histopathological changes of scleroderma in 1924. O'Leary and Nomland elaborated the distinctive features of Systemic sclerosis versus Morphea in an extensive clinical study in 1930[5].

DEFINITION

Systemic sclerosis is a multisystem disease characterized by

1. autoantibodies
2. vascular abnormalities
3. connective tissue sclerosis
4. atrophy

DIAGNOSTIC CRITERIA

American College of Rheumatology (ACR, formerly American Rheumatism Association) Subcommittee for Scleroderma have established the diagnostic criteria for Systemic Sclerosis, according to which patient should have one major criterion or two out of three minor criteria [6]

A. Major criterion

Proximal scleroderma: Symmetric thickening, tightening, and induration of the skin of the fingers and the skin proximal to the metacarpophalangeal or metatarsophalangeal joints, affecting limbs, face, neck or trunk

B. Minor criteria

1. Sclerodactyly

2. Digital pitting scars

3. Bibasilar pulmonary fibrosis

This criteria is 97% sensitive and 98% specific for the diagnosis.

The ACR has proposed an expanded list of criteria,

including:

1. Skin changes which include tightness, thickening, and nonpitting induration, sclerodactyly, proximal scleroderma; changes proximal to the metacarpophalangeal or metatarsophalangeal joints, and affecting other parts of extremities, face, neck, chest, abdomen, digital pitting, loss of substance from finger pad, bilateral firm but pitting finger or hand edema, abnormal skin pigmentation (salt and pepper pigmentation).The changes are usually bilateral, symmetrical and almost always include sclerodactyly.

2. Raynaud's phenomenon: at least two-phase color change in fingers and often toes consisting of pallor, cyanosis, and reactive hyperemia.

3. Visceral manifestations: bibasilar pulmonary fibrosis not attributable to primary lung disease, lower (distal) esophageal dysmotility, colonic sacculations

CLASSIFICATION

Patients are classified as [7]

i) diffuse cutaneous systemic sclerosis (dSSc)

ii) limited cutaneous systemic sclerosis (lSSc)

Diffuse cutaneous systemic sclerosis

- Short interval (<1 year) between the onset of Raynaud's phenomenon and the development of skin changes
- Peripheral and truncal skin involvement
- Tendon friction rub
- Pulmonary fibrosis, renal, gastrointestinal and myocardial involvement
- Capillary drop-outs in nail folds
- Anti Scl-70 - positive
- Anticentromere antibody (ACA) - negative

Limited cutaneous systemic sclerosis

- Long history (1 yr duration) of Raynaud's phenomenon
- Only peripheral skin involvement
- Calcification, telangiectasia, late onset of pulmonary arterial hypertension
- Capillary dilatation in nail folds
- Anticentromere antibody(ACA) - positive

EPIDEMIOLOGY

Systemic sclerosis is a connective tissue disease with worldwide distribution and affects all races. Incidence varies between 2.3 and 10 per million population[8]. The prevalence rates according to a British study were 13 and 48 per million males and females respectively[9]. Estimates of prevalence in South Carolina are higher (67–265 per lakh population)[10]. The incidence and prevalence in the US are approximately 20 and 250 cases per million population, respectively.

Women are affected more often than men. Ratio of males to females is between 1: 3 and 6[11]. In men, a number of occupational associations have been reported, especially miners and stonemasons[12]. This suggests pneumoconiosis and silicosis could be predisposing factors for Systemic sclerosis.

Age of onset in women peaks at fourth decade and but in men it is still later. 85% of patients with Systemic sclerosis are between the ages of 20 and 60 years. Systemic sclerosis can occur in children and elderly.

Black patients have an earlier mean age of onset and more likelihood for diffuse disease[14].

Approximately 1.5% patients have one or more affected first-degree relatives. This represents a 10- to 15-fold higher risk of Systemic sclerosis in family members than in the general population. This supports the role of genetics in disease pathogenesis.

Parameters predicting a worse prognosis include male sex, black race, onset at older age, systemic involvement at the time of diagnosis, skin fibrosis involving the trunk, and elevated ESR.

ETIOLOGY

Etiology of the disease is unknown. And hence several etiological factors have been hypothesized.

Genetic factors

Familial cases of Systemic sclerosis is rare. Less than 5 % concordance is seen in twin studies. But the incidence of antinuclear antibodies among family members is high suggesting the possibility of genetic role in pathogenesis of the disease[13].

HLA-DR typing show an increase in HLA DR2, DR3 and DR5. The presence of HLA B8-DR3-DR52-DQB2 haplotype predisposes to pulmonary involvement, interstitial lung disease. Raised DR2 and DR5 was seen in patients with mild disease and presence of anticentromere antibodies.

Genetic polymorphisms of the candidate genes – POLR3A, CXCR2, TGF β, SPARC, ACE, fibrillin 1, COL1A2 have been identified.

There is increased frequency of microchimerism in Systemic sclerosis patients[16]. Microchimerism occurs due to transfer of fetal cells to the mother or maternal cells to the fetus. This might trigger autoimmunity.

Female preponderance suggest that the genotype involved is a dominantly inherited allele present in the X chromosome.

Age of onset depends on the time of occurrence of specific random events that is possibly the somatic mutations in lymphoid stem cells. This leads to production of 'forbidden' clones. The forbidden clones produce autoantibodies which are pathogenic and damage the endothelial cells. After a latent period, damage occurs to the tissues occur.

Immunological factors

Antinuclear antibodies is present in over 80% of patients. Anti-topoisomerase I antibodies is seen in 22% of patients and anticentromere antibodies in up to 30% of patients.

Anti-RNA polymerase III antibody is associated with renal crisis in about 20 % of cases. U1 RNP antibody is seen in overlap syndrome – mixed connective tissue disorder.

These facts suggest the possibility of autoimmune mechanism. But it is not yet clear if antibodies are the primary abnormality or they result from cellular damage.

Environmental factors

Several substances have been identified as risk factors involved in the causation of the disease. It is found in the studies that men are at higher risk of acquisition of scleroderma following occupational exposure.

- Silica –the most commonly implicated substance which is found in the earth and several other products. But it is the inhalation of crystalline silica which causes autoimmune disorders like Systemic sclerosis, SLE[12].
- Solvents like benzene, trichloroethylene, paint thinners and removers[18]
- Polyvinylchloride[17]
- Pesticides - heptochlor, malathion, parathion, DDT, sodium dinitro-orthocresolate and 7-chlorocyclohexane[19]
- Dental amalgam containing mercury
- Epoxy resins[20]
- Firework - heavy metals like Aluminium, Antimony, Barium, Copper, Iron, Magnesium, Lithium, Zinc, Gold [21]

Drugs

Bleomycin[22], Carbidopa [23] , Paclitaxel , Cocaine[25], pentazocine [24] have been implicated in causing scleroderma and Raynaud's phenomenon.

PATHOGENESIS

The key components involved in the pathogenesis are

1. microvascular dysfunction and damage
2. immune activation with autoantibody production
3. fibrosis of tissues

Vascular

Vascular dysfunction and endothelial injury represent early events in the pathogenesis of the disease. Vasculopathy is due to

- Altered balance between vasoconstrictors (e.g. endothelin) and vasodilators (e.g. nitric oxide)
- endothelial cell apoptosis[26]
- intimal proliferation progressing to luminal occlusion
- defective angiogenesis

Resultant hypoxia leads to synthesis of profibrotic cytokines, fibroblast activation and collagen production.

Raynaud's phenomenon is caused by both

- reversible vasospasm
- irreversible arterial damage - intimal proliferation and luminal obstruction

Endothelial damage is reflected in abnormal capillary loops and avascular areas in the proximal nail folds as well as the development of telangiectasias. Endothelial injury lead to vascular leak and edema, which characterize the early oedema phase of cutaneous involvement. Vascular abnormalities play a major role in the pathogenesis of renal crisis and pulmonary hypertension.

Fibrosis

Stimulation of fibroblasts by cytokines and growth factors lead to fibrosis of tissues[27]. TGF – β[28] and CTGF [29] constantly stimulate the fibroblasts and result in sustained production of collagen. The fibroblast is hence in a profibrotic microenvironment.

The accumulation of collagen in Systemic sclerosis seems to be primarily the result of increased synthesis, rather than decreased degradation.

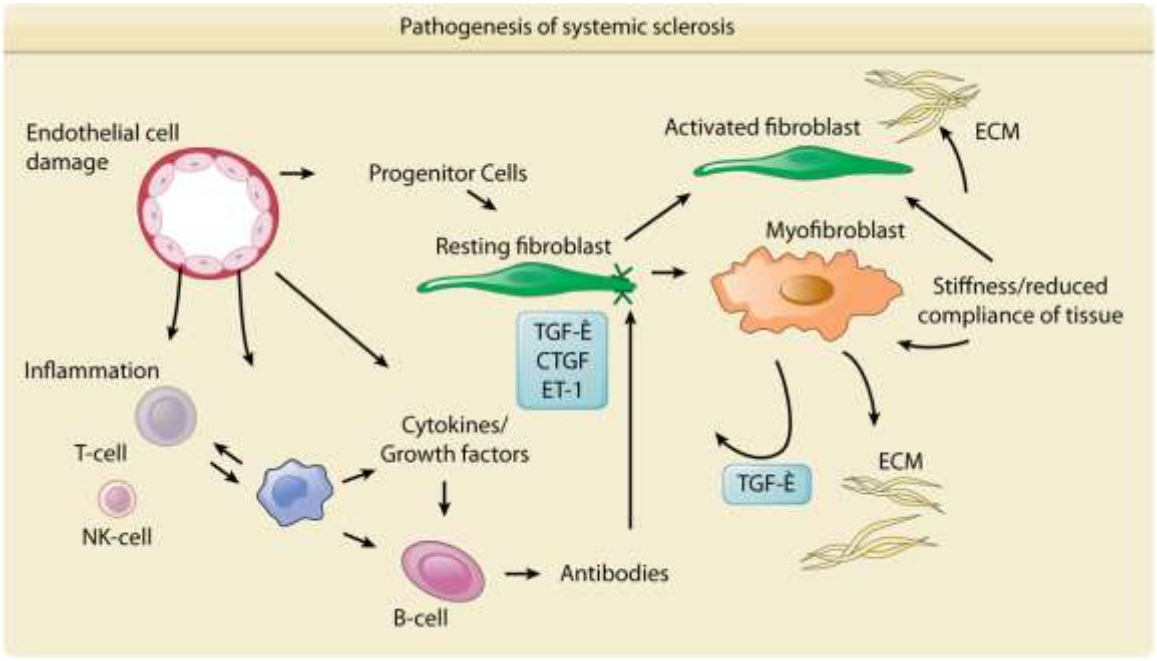
Though there is no direct evidence of cytokines involved in fibrosis, it is possible that improvement may occur by inhibiting the cytokines.

Immune activation

Factors favouring immunological role in Systemic sclerosis

- The presence of autoantibodies supports a role for immune system activation
- Topoisomerase I–antitopoisomerase I complexes attached to fibroblast stimulate monocyte adhesion
- antiendothelial antibodies trigger endothelial cell apoptosis[30]
- antibodies against PDGF receptor induce expression of type I collagen in fibroblasts
- clonal T-cell expansion seen in lesional skin indicates an antigen-driven response
- Lymphocytic infiltrates have been observed in the skin as well as the lungs
- T cells show a predominant Th2 profile with increased secretion of profibrotic cytokines such as IL-4
- Expansion of naive B cells and chronic activation, but there is decreased number of memory B cells
- Similar clinical features in chronic GVHD.

It is clear from the above facts that immune system is affected. But immunosuppressive drugs have failed in producing disease-modifying responses and this raises questions regarding its role. Perhaps immunologic events occur only in the early phase.



CLINICAL FEATURES

SKIN MANIFESTATIONS

1.Skin tightness

Skin undergoes three phase change

- early edematous phase - pitting edema of the digits
- sclerotic phase - taut, shiny appearance, immovable or hidebound due to binding down of skin to the deeper structures
- atrophic phase - gradual softening of the skin

The hands and face are most commonly involved and extends proximally to involve the forearms and arms. The fingers become semiflexed, immobile and useless, the skin over the fingers become hard, inelastic, palid and incompressible. Distal phalanges are boardlike and indurated.

Mizutani described the "round finger pad sign"[31]. Due to loss of pulp on digit, fingers appear as rounded hemisphere rather than normal peaked contour when viewed from side. This is more appreciated in ring finger. This is not only seen in systemic sclerosis but also in MCTD, severe Raynaud's phenomenon with sclerodactyly.

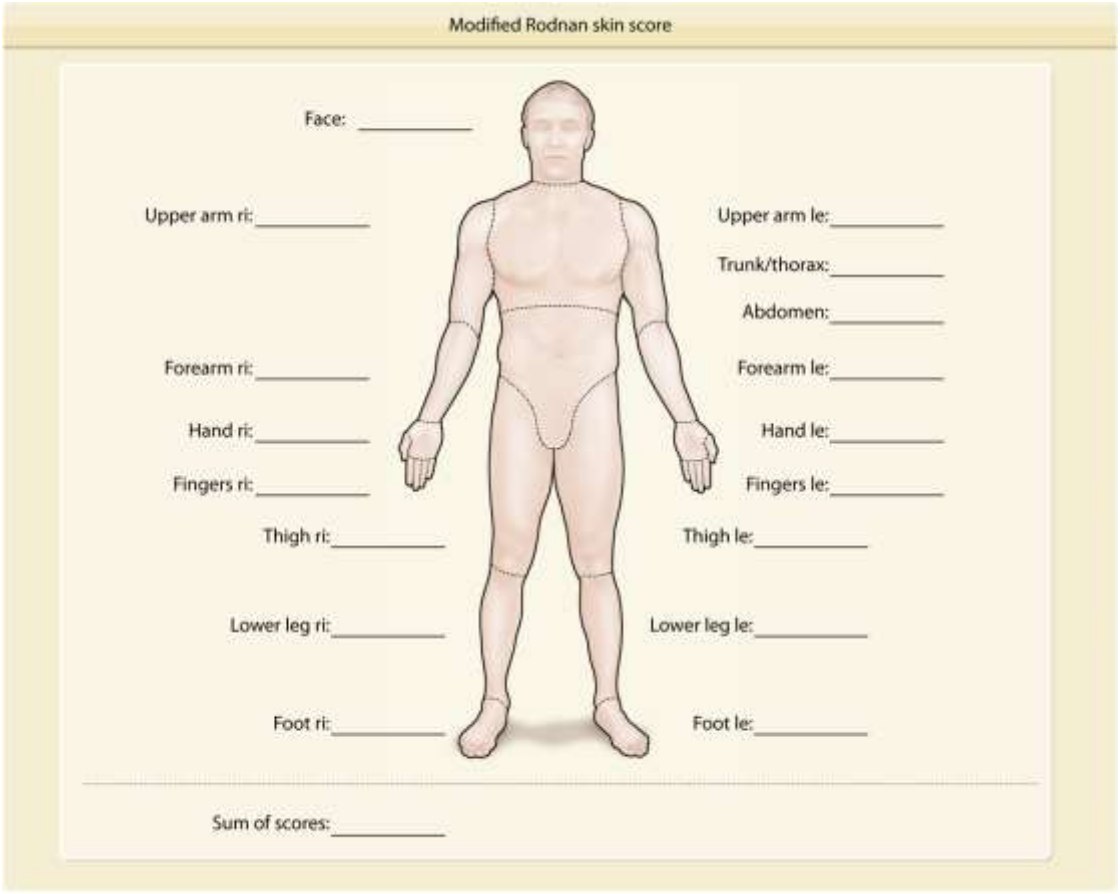
Face is drawn, stretched and masklike with loss of lines of expression. Forehead is smooth, shiny and taut, nose becomes sharp and pinched, mouth opening is restricted and radial furrows and thin lips gives a pursed mouth appearance.

Oral aperture becomes drastically reduced and interferes with eating and maintain oral hygiene. The lower eyelids cannot be retracted to visualize tarsal conjunctivae due to atrophy of the tissues. A. J. Barnett[32] described " neck sign" which is ridging and tightening seen on extension of neck. This is found in 90% of cases and is due to adherence of skin to the platysma which interfere with neck extension.

Chest is tight, shiny and pigmented. Severe involvement leads to cuirasse like restraint of respiration. In feet, less severe changes occur, but not infrequently black toes with incipient gangrene occur. The feet becomes encased in tight, firm and taut skin with pigmentory changes and atrophy. The skin changes can extend upto the thighs. Skin thickening and fibrosis adjacent to tendons lead to contractures at elbow, wrist and knees.

A very small group of patients develops vascular, immunologic, and organ-based fibrotic features of Systemic sclerosis without skin sclerosis. They constitute approximately 1 percent of Systemic sclerosis cases and are termed Systemic sclerosis sine scleroderma.

The extent and severity of skin involvement can be evaluated by Modified Rodnan Skin Score (MRSS). Usually, 17 sites are assessed by palpation of the skin by a trained examiner and skin thickness is categorized to grade 1, 2, or 3, corresponding to mild, medium, and severe. Maximum skin score being 51. Skin score at baseline correlates with disease severity and outcome.



2. Raynaud's phenomenon

Raynaud's phenomenon is characterized by episodic vasospasm of the arteries of digits. In some patients it may affect the tip of nose and earlobes. Exposure to cold, precipitates the attack; frequency and severity of attacks is more in winter. Typical attack starts as pallor, followed by bluish discoloration. Eventually erythema occurs spontaneously or on rewarming. Pathogenetic mechanisms of colour change is vasoconstriction, ischemia, and reperfusion. Some experience only pallor or cyanosis. Primary Raynaud's phenomenon represents an exaggerated physiological response to cold and is not associated with underlying disease. Secondary Raynaud's phenomenon occurs with underlying connective tissue disorder, endocrine conditions, occupation involving vibratory tools, medications and malignancy. It is more severe, frequent, prolonged and painful and is associated with ischemic lesions and gangrene of digits.

It is the earliest symptom to appear in Systemic sclerosis. Raynaud's phenomenon may be present for months or years before the skin changes appear. The duration is shorter in males, usually less than one year[33]. In females, it is around five years, but may be longer upto thirty years.

Raynaud's phenomenon can be absent, can occur simultaneously, or occur after the onset of skin changes. In Diffuse cutaneous systemic sclerosis, the interval between the onset of Raynaud's phenomenon and skin changes is shorter, less than one year. In Limited cutaneous systemic sclerosis the interval is longer. Sclerodactyly may be present in 10% of cases with Raynaud's disease, but the occurrence of systemic sclerosis is rare. Nail fold capillaroscopy and autoantibody testing are helpful in differentiating Raynaud's disease and systemic sclerosis[34].

3. Fingertip ulcers

Small painful fingertip ulcers are common finding and difficult to treat. Ulcers are due to ischemia, fibrotic tissue and trauma. Ulcers on the interphalangeal joints are likely to persist because of continued trauma. They heal leaving behind depressed stellate scars.

Pitted scars occur not only on the tips of the fingers but also on the ulnar border of thumb, radial borders of index and middle fingers and dorsa of the finger joints. Ulcers can lead to osteomyelitis and autoamputation. They are painful and limit the use of the fingers and hands thereby decreasing the ability to perform activities of daily living and can lead to the depression. Gangrene of the digits is not uncommon and can occur early in the disease.

4. Pigmentary changes

Diffuse hyperpigmentation is the most common pigmentary change. Pigmentation occurs in about half of the patients, most common site being face and less commonly present in legs, thighs, lower abdomen, axilla. Patients appear to be tanned, and the hyperpigmentation is more pronounced in areas of pressure such as the belt line or under brassiere. Sometimes the pigmentation may be extensive and lead to the suspicion of Addison's disease.

The leukoderma is characterized by localized areas of depigmentation with sparing of the perifollicular skin; described as the 'salt and pepper' sign. It is common in scalp, upper back and chest. Perifollicular pigmentation may appear in response to UV exposure. Pigment may also be retained in the skin overlying superficial veins (perivenular retention of pigment).

5. Nail changes

Nail in later stages becomes very small and seen curving over the terminal phalange. The nail fold frequently shows ragged cuticles.

Pterygium lnversum unguis may occur where the distal part of the nailbed is adherent to the ventral surface of the nail plate. Paronychia and Slow healing whitlows are common.

Dilated, nailfold capillary loops are present in 90% of systemic sclerosis patients[34]. Use of an ophthalmoscope or dermascope may enhance appreciation of the changes.

In diffuse cutaneous Systemic sclerosis nail folds show capillary drop-out. In limited cutaneous Systemic sclerosis nail folds show capillary dilatation.

The changes occur symmetrically in systemic sclerosis. This differentiates it from the nailfold capillaries of the Osler-Weber- Rendu syndrome which typically have dilatation of only one half of the loop and no avascular areas.

Nailfold capillary hemorrhage in two or more fingers is highly specific for limited cutaneous Systemic sclerosis and correlates with the anti centromere antibody.

6.Telengiectasia

Telangiectasias are more common in patients with limited type Systemic sclerosis but can also occur in diffuse type Systemic sclerosis. Size varies from 2 mm to 2 cm in diameter, blanches on pressure.

They are frequently found on the face, chest and hands. These telangiectatic macules are said to be matted or squared-off, which differentiates it from the raised lesions associated with hereditary hemorrhagic telangiectasia.

7. Calcinosis cutis

Weber [35]first described occurrence of calcinosis cutis in systemic sclerosis long before Thibierge and Weissenbach[36]. Calcinosis is a late manifestation of Systemic sclerosis and is common in limited type.

It made of calcium hydroxyapatite and can be found in the fingertips, and muscles. This is usually present in cases with dermatomyositis overlap.

Calcinosis usually seen at the areas prone for trauma like the extensor surfaces of forearm and fingers. These calcifications can ulcerate discharging chalky material and sometimes leading to secondary infection.

The pathogenesis is still not clear, probably induced by tissue damage, hypoxia and physical trauma. Calcification can occur in the internal organs also.

Other skin changes

- cobble stone appearance in skin – multiple small papules of telengiectasia occur due to lymphatic obstruction by sclerosing process
- Hypohidrosis of skin leads to dryness of skin and pruritus can be marked.
- Fibrotic skin shows diminished hair growth and hypertrichosisis common in the recovery phase.
- Vesicles and bullae may occur especially in distal extremities
- Leg ulcers can occur and are slow healing and difficult to treat
- Livedo reticularis
- Atrophie blanche
- Erythema nodosum like nodules
- Hyperkeratotic plques over the phalanges
- Erythema over thenar and hypothenar eminences
- Chondrodermatitis nodularis helicis

OVERLAP SYNDROMES

Group of disorders showing features of two or more autoimmune connective disorders

- Systemic sclerosis
- Polymyositis or dermatomyositis
- Systemic lupus erythematosus
- Sjögren syndrome
- Vasculitis
- Polyarthritis
- Rheumatoid arthritis

Some association occur more frequently than others. For instance, systemic sclerosis is more often associated with dermatomyositis than systemic lupus erythematosus. The disease can occur concurrently or consecutively.

Recently antibody markers are being identified in these subsets with particular pattern of disease as mentioned below. Identification of antibodies and subsets not only provides information about prognosis and treatment but also provides clues for identifying antigen targets and about etiopathogenesis.

- anti-U1-ribonucleoprotein – mixed connective tissue disease - systemic lupus erythematosus, systemic sclerosis or myositis
- anti PM-Scl, anti Ku, U2-ribonucleoprotein - systemic sclerosis and polymyositis
- anti-Jo-1 - polymyositis and pulmonary fibrosis

MIXED CONNECTIVE TISSUE DISEASE

Sharp et al [37] in 1972 described in a group of patients with clinical features of SLE, Systemic sclerosis, myositis association with antibody to U1 ribonucleoprotein (RNP).

It is reported in all races and there is no difference in clinical presentation among various ethnic groups.

More common in females, the ratio of male to female being 1:3. Onset of disease can occur at any age, more commonly between 15 and 25 years.

Clinical features are Raynaud's phenomenon, joint involvement, sclerodactyly, oesophageal dysmotility, myositis, pulmonary hypertension, swelling of hands, malar rash, pleuritis and pericarditis. Renal involvement is present clinically in 5 % of cases.

Neuropsychiatric manifestations occur in about 15 % of cases and include trigeminal neuralgia, aseptic meningitis, transverse myelitis and psychosis.

A study based on large single-center cohort of MCTD patients suggests that 3 clinical subclusters of MCTD manifestations may exist[38]

- Patients with predominant vascular manifestations, like Raynaud's phenomenon, pulmonary hypertension and antiphospholipid syndrome with thromboses. These patients are at the greatest risk of mortality.
- Patients with polymyositis like picture, including interstitial lung disease, oesophageal dysmotility and myositis
- Patients with erosive polyarthritis with antibodies to CCP (cyclic citrullinated peptides) and sclerodactyly.

MCTD is more severe in children, often with arthritis, renal, cardiac involvement. Thrombocytopenia may be present in children. But the overall prognosis is quite good.

The disease responds well with corticosteroids. Other treatment options include hydroxychloroquine and methotrexate and have been reported to be successful. Prognosis is generally better than that of Systemic sclerosis. Antibody U1 RNP gets suppressed on treatment and disappears when the patient is in remission [39].

SYSTEMIC INVOLVEMENT

GASTROINTESTINAL INVOLVEMENT

Gastrointestinal tract is involved in 90% of patients[40]. Underlying pathology – prominent atrophy and fibrosis of smooth muscle, obliterative vasoculopathy lead to abnormal motility of oesophagus, stomach and intestine.

Oesophagus is the most frequently involved part of the gastrointestinal tract affecting upto 75 % of the cases. Gastroesophageal reflux disease (GERD) starts early and presents with heartburns, regurgitation of food and dysphagia. It is due to reduced lower oesophageal sphincter pressure, abnormal motility of lower two- third of the oesophagus and delayed emptying of stomach. Chronic GERD leads to complications like strictures, Barrett's oesophagus and adenocarcinoma. Extra – oesophageal complications include hoarseness of voice, chronic cough and aspiration pneumonitis[40]. Dysphagia occurs due to loss of propulsive peristalsis, oesophagitis and candidial infection. Localized dysphagia involving the neck region can occur because of thickened pharyngo- oesophageal muscles[41]. Oesophageal aperistalsis and diffuse spasm have been reported.

Stomach is rarely involved in about 6 % of cases, in Asians the incidence is higher. Gastroparesis causes early satiety, abdominal distension and pain, and aggravates GERD. Telengiectasia can occur throughout the GIT and can cause bleeding. Gastric antral vascular ectasia are subepithelial lesions and may cause recurrent occult bleeing leading to anaemia. Endoscopy shows striped appearance and hence called watermelon stomach.

Small intestinal dysmotility results in stagnation of food eventually leading to bacterial overgrowth causing diarrhea and malabsorption. Malabsorption of fat, protein, calcium, folic acid and vitamin B12 ensue, sometimes leading to severe malnutrition. This can be treated with tetracyclines. Disturbed intestinal motor function also causes pseudoobstruction of the intestines. Clinical features include acute abdominal pain, nausea and vomiting. Diagnostic challenge in distinguishing it from true obstruction. Pseudobstruction responds to supportive care and intravenous nutrition. Pneumatosis cystoides intestinalis occur due to air trapping in bowel wall[42]. Cysts can rupture resulting in pneumoperitoneum. Pancreatic necrosis and volvulus can rarely occur. Colon involvement can cause constipation, diarrhea, rectal prolapse, volvulus. Wide mouth diverticula can rarely perforate or bleed.

PULMONARY INVOLVEMENT

Respiratory symptoms in scleroderma lung disease can be quite nonspecific. The fact that the pulmonary manifestations are the leading cause of morbidity and mortality prompts the efforts to detect the respiratory involvement as early as possible [44]. The precise staging and the timely institution of therapy influence the outcomes of scleroderma.

Dyspnea on exertion is the symptom usually first noticed, but with progression it is also present at rest. The cough is often dry and nonproductive. The tightness of chest is often reported, along with some nonspecific symptoms like fatigue.

Dyspnea could be due to ILD or due to some infrequent pulmonary manifestations, such as bronchiectasis/bronchioloectasis, diffuse alveolar hemorrhage. Sometimes the causes may be extrapulmonary like cardiac involvement, especially the left ventricular diastolic dysfunction, diminished thoracic cage expansions, neuromuscular, and pleural disease.

The involvement of the lungs in scleroderma may be detected by auscultation, as in some patients the bibasilar late inspiratory fine crackles are identified. Physical examination reveal loud P2, and ejection systolic murmur over left sternal border. Tricuspid regurgitation, hepatomegaly, ascites, and edema are signs of corpulmonale.

ILD is most frequent among pulmonary manifestations. Though pulmonary fibrosis is more associated with Diffuse cutaneous scleroderma, it can occur in limited cutaneous forms and scleroderma sine scleroderma.

Pulmonary arterial hypertension

Incidence is about 8 – 10 % in scleroderma patients [44]. Although it occur in both limited and diffuse cutaneous subsets, the most cases are of limited cutaneous Systemic sclerosis. This condition has features similar to idiopathic PAH.

Two patterns of pulmonary hypertension occur in Systemic sclerosis.

1. primary PAH
2. secondary Pulmonary Hypertension – seen in late-stage extensive interstitial lung fibrosis, they develop a true secondary PH.

It is important to distinguish both as fibrosis is also present in cases of PAH. If lung volume is less than 60% of the predicted value, pulmonary hypertension is more likely to be secondary to pulmonary fibrosis.

Exertional dyspnoea is the main symptom. Fatigue, chest pain and edema are features of right heart failure. Prognosis was worse pretreatment era. The three year survival rate is around 30 %. But the prognosis of PAH due to Systemic sclerosis is better than idiopathic PAH.

RENAL INVOLVEMENT

Most frequent findings include chronic nonprogressive proteinuria and hypertension. The most dreaded complication, scleroderma renal crisis occurs in 20% of patients. The pathogenesis involves obliterative vasculopathy of renal cortical arteries leading to reduction in blood flow. This is aggravated by vasospasm leading to activation of renin angiotensin axis and further vasoconstriction cycle resulting in malignant hypertension. Precipitating factors include dehydration and hypotension. Risk factors are male, diffuse involvement, African – American race [46].

Patients with malignant hypertension present with sudden onset of severe headache, blurring of vision, chest pain. In 10 % cases, blood pressure remains normal, this is described as normotensive renal crisis. Urine examination shows proteinuria, hematuria. Peripheral blood smear shows thrombocytopenia and fragmented RBCs.

Aggressive management with ACE inhibitors improve the prognosis [45].

CARDIAC INVOLVEMENT

Scleroderma can involve all structures, endocardium, myocardium, pericardium individually or together. Cardiac involvement is often silent but can be detected by sensitive diagnostic tools.

Cardiac involvement is more common in diffuse cutaneous systemic sclerosis [43]. Manifestations include

- Pericardial effusion
- Conduction abnormalities
- Rhythm abnormalities - Atrial & ventricular tachycardia
- Pulmonary arterial hypertension
- Mitral valve prolapse
- Cardiac failure
- Valvular regurgitation
- Hypertrophic cardiomyopathy

Cardiac involvement develops early in the disease usually within three years of onset of skin thickening. Clinically evident cardiac involvement has poor prognosis.

BONE INVOLVEMENT

Acroosteolysis (i.e. resorption of the distal end of the phalanx) may occur due to long-standing digital ischemia. Sometimes it affects other sites, including the mandibular condyles, the distal radius, and the superior portion of the posterior ribs. In scleroderma, acral osteolysis can occur with calcinosis, this differentiates it from Raynaud's phenomenon where only acral osteolysis occurs[47].

Other bone changes in scleroderma include juxta-articular osteoporosis, osteopoikilosis[48], and avascular necrosis of the femoral head.

MUSCLE INVOLVEMENT

Myopathy can occur in two different forms[49]

- Noninflammatory fibrotic myopathy (60%–80%) - characterized by mild weakness and a minimally elevated creatine kinase
- Inflammatory myositis (6%–12%) - elevated levels of serum creatine kinase and aldolase, and PM-Scl antibodies, indistinguishable from polymyositis.

The muscles of the forearms and hands are involved as well as the proximal muscles.

The juxta-articular tendons of the fingers, forearms, legs, and neck can be altered by fibrosis causing audible friction rubs as the tendon is moved actively or passively.

JOINT INVOLVEMENT

Generalized arthralgias and morning stiffness affecting both small and large joints often precedes skin changes. In diffuse scleroderma, rapid development of hand swelling and sclerotic changes can lead to severe flexion contractures with claw-like hand deformities and severe disability.

CENTRAL NERVOUS SYSTEM

Involvement is seen in around 10% patients. Manifestations [50] include

- Trigeminal neuropathy occurs in 4% of patients. It presents with pain and numbness over the face. It is initially unilateral, later becomes bilateral.
- Brachial plexopathy
- Carpal tunnel syndrome
- Meralgia paraesthetica
- Lumbosacral radiculopathy
- Subacute combined degeneration due to deficiency of vitamin B12
- Spinal cord compression as a result of soft-tissue calcification.
- Prolongation of sensory chronaxia - both abnormal and normal skin.
- Duration of action of local anaesthetics is prolonged

DENTAL CHANGES

Stafne's sign - Widening of the periodontal membrane is present in about 30% of patients[51]. It is not a diagnostic sign as it is also seen in periapical infection. In periapical infection, it is present in only one teeth.

EYE INVOLVEMENT

Eyes changes [52] include

- Tightness of the eyelids
- Shallow fornices
- Diminished tear secretion
- Keratoconjunctivitis sicca
- Retinopathy – due to direct vascular involvement

Sjögren's syndrome is seen in 15% of cases.

GENITAL TRACT INVOLVEMENT

Dryness of vagina, ulcers lead to painful intercourse and decreased sexual satisfaction [53]. This often results in decreased frequency of intercourse.

CHILDHOOD SYSTEMIC SCLEROSIS

Systemic sclerosis is rare in children,they make up only 3% of all cases of scleroderma. Clinical features resemble those of adults. However Raynaud's phenomenon, dilatation of nailfold capillary, digital ulcers, pitting scars, and telangiectasia are less frequently seen.

The course in childhood is slower and systemic involvement is less severe. Renal involvement is rare [54].

Pulmonary disease is almost universal in children with Systemic sclerosis and High resolution CT scanning is sensitive and appropriate for younger children who cannot perform pulmonary function tests. Because early aggressive treatment may improve the outcome, patients with pulmonary disease, high resolution CT scanning should be performed in patients and should be monitored annually for its development.

Symptoms of gastrointestinal reflux (GERD) and oesophagitis may not be reported by children. Therefore children may need to be evaluated for acid reflux even in the absence of clinical symptoms.

In childhood Systemic Sclerosis, ANA is positive in 22% to 100% of patients, and anti-Scl 70 positive in approximately 40% of patients. Antibodies to centromere are uncommon, this reflects the rarity of limited type disease in children

Systemic sclerosis in Pregnancy

- Systemic sclerosis generally remains unchanged throughout the course of pregnancy, but reports of postpartum renal failure and gangrene are present.
- Severe pulmonary, renal or cardiac disease may be an indication for termination of pregnancy. Complications are common in late pregnancy[55].
- ACE - Angiotensin Converting Enzyme inhibitors is helpful for treating hypertension, but this carries potential risk to the fetus.
- Fertility may be impaired.

DIFFERENTIAL DIAGNOSIS – SCLERODERMOID CONDITIONS

The differential diagnosis of dermal sclerosis is extensive. Systemic sclerosis is distinguished by the characteristic symmetrical induration of the skin of distal extremities (especially the upper extremity), nailfold capillary changes, Raynaud's phenomenon, autoantibody profile and internal organ involvement.

Immunological

Morphea

Eosinophilic fasciitis

Chronic GVHD

Metabolic

Diabetic cheiroarthropathy

Porphyria cutanea tarda

Phenylketonuria

GEMSS syndrome – glaucoma, Ectopia lentis , Microspherophakia, Stiff joints and Short stature *syndrome*

Mucinosis

Scleredema

Scleromyxoedema

Toxin mediated

Nephrogenic systemic fibrosis

Toxic oil syndrome

Eosinophilia myalgia syndrome

Drug or chemical

Bleomycin, carbidopa, pentazocine, cocaine, Taxanes

Vinyl chloride, chlorinated hydrocarbons, benzene, toluene, epoxy resins

Venous insufficiency

Lipodermatosclerosis

Genetic

Hutchinson – Gilford syndrome

Werner Syndrome

Stiff skin syndrome

Huriez syndrome

Ataxia telangiectasia

Neurological

Reflex sympathetic dystrophy

Spinal cord injury

Paraneoplastic

POEMS syndrome

Primary amyloidosis

Carcinoid syndrome

Neoplastic

Carcinoma en cuirasse

INVESTIGATIONS

- **Acute-phase reactants**
  - is raised if patient has synovitis, tendon friction rub, arthritis
- **Complete blood count**
  - Anaemia
    1. iron deficiency anaemia – due to recurrent Gastrointestinal bleeding
    2. Anaemia of chronic disease
    3. Vitamin B12/ folic acid deficiency – caused by malabsorption due to hypomotility and bacterial overgrowth
    4. Microangiopathic hemolytic anemia – fragmented RBCs seen in scleroderma renal crisis[46]

AUTOANTIBODIES

Antinuclear antibodies is positive in 80 –90% of patients with Systemic sclerosis. It is still not clear whether antibodies have a direct role in pathogenesis or they are occur as an epiphenomenon.

The antibodies classically associated with Systemic sclerosis [57]are

- ACA (Anticenteromere antibodies)
- antitopoisomerase I or anti-Scl-70.

ACA is seen in limited cutaneous Systemic sclerosis and antitopoisomerase I is seen in diffuse cutaneous Sytemic sclerosis.

Less commonly associated antibodies – disease specific[57]

- anti-PML-Scl
- anti-Th/To
- antifibrillarin /anti-U3 ribonucleoprotein
- anti-RNA polymerase

less commonly associated antibodies – disease nonspecific[57]

- anti-Ku
- anti-Ro
- antiphospholipid
- anti-U1RNP
- anti-Sm antibodies

Anticentromere Antibody

The Anticenteromere antibodies [57] is positive in 20 to 30 % of patients with Systemic sclerosis. They are present in around 50% of patients with the limited type of Systemic sclerosis, but in less than 5% of patients with the diffuse form of disease. They are strongly associated with the CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactly and telangiectasia). When found in patients with Raynaud's phenomenon they predict the development of Systemic sclerosis. The presence of Anticenteromere antibodies carries a better prognosis.

Antitopoisomerase-I Antibodies (Anti-Scl-70 Antibodies)

They are seen in up to 40% of patients with diffuse cutaneous Systemic sclerosis and less than 10% of patients with limited cutaneous Systemic sclerosis [57].

When present in a patient with Raynaud's phenomenon, they predict the risk of developing Systemic sclerosis. Anti-Scl-70 antibodies are associated with interstitial lung disease (ILD).

ACA and anti-Scl 70 exist in isolation and are rarely found together

Antinucleolar Antibodies

- Anti-PM-Scl antibodies [57]

  – 50% of cases with polymyositis/scleroderma overlap syndrome.

  - 2–3% of cases with Systemic sclerosis

  - 8% of cases with myositis.

- Anti-Th/To antibodies[57]

  Antibodies are directed against the ribonuclease mitochondrial RNA processing complex (MRP) and ribonuclease P complexes.

  They are found in about 2–5% of patients with Systemic sclerosis and show racial difference being more commonly found in Japanese patients. They have also been seen in patients with SLE and PM. Similar to Anticenteromere antibodies they indicate limited type disease.

- The anti-RNA polymerase group (I and III) – 20 %

  Associated with diffuse type of Systemic sclerosis and correlates with pulmonary arterial hypertension (PAH).

- Antifibrillarin antibodies [57] - 4% diffuse type of disease with myositis, PAH and renal involvement.

Other Autoantibodies

- Anti-Ku antibodies - Overlap syndrome - SLE and systemic sclerosis
- Anti-Ro antibodies - Systemic sclerosis with Sjögren syndrome.
- Anti-Sm antibodies – Systemic sclerosis with features of SLE and renal involvement.
- Anti-U1-RNP antibodies – Mixed connective tissue disease (MCTD) – features of Systemic sclerosis, SLE, dermatomyositis. They have a favourable prognosis
- Anticardiolipin antibodies are present in about 20–25% of patients

SKIN BIOPSY

Skin biopsy is not routinely done and is rarely indicated as the diagnosis is made clinically based on the ACR criteria

It may be of help in atypical presentations of disease and in differentiating from conditions mimicking Systemic sclerosis.

Histopathology of morphea and systemic sclerosis are identical and is not possible to differentiate both histolgically.

Biopsy shows a thinned epidermis and extensive fibrosis of the lower two-thirds of the dermis and extending into the panniculus, replacing the subcutaneous fat. A perivascular mononuclear cell infiltrate may precede fibrosis. The collagen bundles appear pale, homogeneous and swollen. In later stages, a significant inflammatory cell infiltrate is not observed; this is in contrast to morphea, where a prominent inflammatory cell infiltrate is present. The number of adnexal structures is reduced, another characteristic feature, and the epidermal rete ridges are effaced [58].

Direct immunofluorescence is usually negative in Scleroderma.

Pulmonary Function Tests :

Pulmonary function tests play a crucial role in evaluation of pulmonary involvement in scleroderma.

Up to 40% of scleroderma patients show at least a moderate restrictive pattern in spirometry, and 15% have severe restriction without obstruction. Diffusion capacity for carbon monoxide (DLCO) is more sensitive in detecting lung involvement than forced vital capacity (FVC), but less specific for ILD as pulmonary vascular disease and COPD emphysema may also cause decreased DLCO[59].

Impaired DLCO correlates with severity of ILD, measured as the extent of the disease on computed tomography. Baseline values of DLCO and FVC have been used to measure disease severity. The decrease in both variables has been associated with increased mortality of patients with ILD in scleroderma. It is to note that disease severity in patients with pulmonary fibrosis due to scleroderma should be classified as mild, moderate, and severe when the measures of DLCO and FVC are 70-79%, 50-60%, and less than 50% of the predicted values. Combination of normally preserved lung volumes and considerably decreased DLCO is characteristic of presence of PAH.

Imaging Studies

Chest X-ray in scleroderma patients with ILD shows linear and

reticular pattern, superimposed upon the ground-glass attenuation. Traction

bronchiectasis may be detected, but contrary to the finding in idiopathic pulmonary fibrosis (IPF), the honeycombing is rare . Evidence of pulmonary disease has been described in chest X-rays in 20–65% of patients affected by scleroderma.

HRCT has improved the diagnosis of ILD due to its high sensitivity. In all scleroderma patients, parenchymal alterations are detected by HRCT in 55–56% of cases, and if they have abnormal pulmonary function tests, the percentage rises up to 91%. The characteristic findings are ground-glass attenuation, reticular, and linear pattern, dominantly on lung bases.

Ground-glass attenuation has been frequently attributed to alveolitis, but it seems that in most cases it presents early phase fibrosis; and only in some cases, it represents the reversible inflammatory disease. It is in accordance with biopsy finding with only less than 25% of scleroderma patients having inflammation, despite ground-glass pattern on HRCT scanning

The honeycombing pattern is not a feature of ILD in scleroderma, although in recent study, it was detected in more than 30% of symptomatic patients,with a significantly higher incidence in patients with limited scleroderma compared to patients with diffuse scleroderma

Ultrasound lung comets (ULCs) [60] is an echographic sign of interstitial lung fibrosis correlates with HRCT findings. This a simple, bedside, radiation-free test.

Bronchoalveolar Lavage (BAL) and Lung Biopsy

The neutrophil with or without eosinophil alveolitis is detected in more than 50% of these patients[61]. It has been shown that high neutrophil count in lung lavage fluid is associated with early mortality, that active alveolitis correlates with more severe lung function, and it also correlates with more extensive fibrosis on HRCT.

Surgical lung biopsy represents a gold standard in the evaluation of ILD as it can show the histopathological type and degree of inflammation and degree of fibrosis. It can also show the presence of other causes of parenchymal involvement. Lung biopsy specimen analysis has demonstrated that the majority of scleroderma-ILD patients show the histopathological pattern of NSIP, less often usual interstitial pneumonia (UIP) or other types of ILD. Most frequent is fibrotic NSIP, where the cellular as well as the UIP variation is quite rare. NSIP is a dominant pathologic pattern in 78% of cases. Bronchiolitis obliterans organizing pneumonia (BOOP) is quite rare pathologic finding, as well as diffuse alveolar hemorrhage.

GASTROINTESTINAL SYSTEM:

Plain radiography images reveals

- bowel dilatation
- intestinal obstruction
- perforation
- Large-mouthed pseudodiverticula seen on the antimesenteric border, mostly in the transverse and descending colon

Barium study of the esophagus – Barium swallow

- Mild to moderate esophageal dilatation
- Hypotonia and diminished peristalsis in the lower two thirds of the esophagus
- lower esophageal sphincter is patulant
- Gastroesophageal reflux
- Erosions and superficial ulcers in the lower esophagus as a result of GERD
- Fusiform stricture 4-5 cm above the gastroesophageal junction as a result of chronic complication of reflux esophagitis
- Barrett esophagus - a fine reticular mucosal pattern is seen distal to the stricture
- Adenocarcinoma – filling defect in barium swallow

Barium study of the small bowel – barium meal

- bowel dilation
- Increased Transit time
- megaduodenum or megajejunum
- pseudodiverticulae/sacculations - asymmetrically distributed squared tops with broad bases on the mesenteric side
- pneumatosis intestinalis intestinal gas dissects into the bowel wall or into the peritoneal cavity, mimicking a perforated bowel.

Computed tomography - abdomen

Indications include

- Oesophageal cancer
- Pneumatosis cystoides intestinalis
- Intestinal obstruction

In pneumatosis cystoides intestinalis is characterized by intramural gas clusters in small and large intestine and pneumoperitoneum.

Ultrasound Abdomen

Assessing involvement in liver in primary biliary cirrhosis associated with scleroderma. Pancreatic involvement can also assessed.

Endoscopy

In Systemic sclerosis, upper GI scopy or Oesophagogastroduodenoscopy is done routinely early in the disease as oesophagitis can occur in asymptomatic patients. OGD shows the presence of dilated lower oesophageal sphincter, oesophagitis, candidial oesophagitis, barrett's oesophagus, stricture.

Biopsy is done in Barrett's oesophagus when there is suspicion of adenocarcinoma.

On sigmoidoscopy, the mucosa of the colon appears pale, dry and rather rigid, but this is very uncommon.

Oesophageal Manometry

Manometry is the gold standard for assessing oesophageal motility disorders.

In most cases, there is low contraction amplitudes in the distal or lower oesophagus. In advanced disease there is weak or aperistalsis of the smooth muscle part of oesophagus and hypotensive lower oesophageal sphincter. Although this pattern is characteristic of scleroderma it is not specific and can occur other conditions including GERD.

Upper oesophagus is not involved in scleroderma, if present associated myositis must be considered, which may be feature of overlap syndrome.

Anorectal pressure measurements show abnormal motility is seen in 74% of patients but most patients are asymptomatic.

Scintigraphy provide a sensitive quantitative index of esophageal dysmotility.

Celiac and mesenteric angiography

It is an accurate way for demonstrating the site and the cause of gastrointestinal bleeding; it also provides the means for therapeutic measures, such as pharmacologic or embolic control of bleeding.

Investigations for renal involvement

- elevated serum creatinine levels – usually the rise is acute, rarely it can be a gradual increase in the levels.
- 24 hour creatinine clearance is less than 60 ml/ min
- Urinalysis – after renal crisis, there is proteienuria usually not exceeding 2g/ day, microscopic hematuria 10- 100 RBC / HPF, granular casts
- Elevated plasma renin levels
- Microangiopathic hemolytic anaemia [56]– peripheral smear shows normochromic fragmented RBCs, schistocytes, reticulocytosis

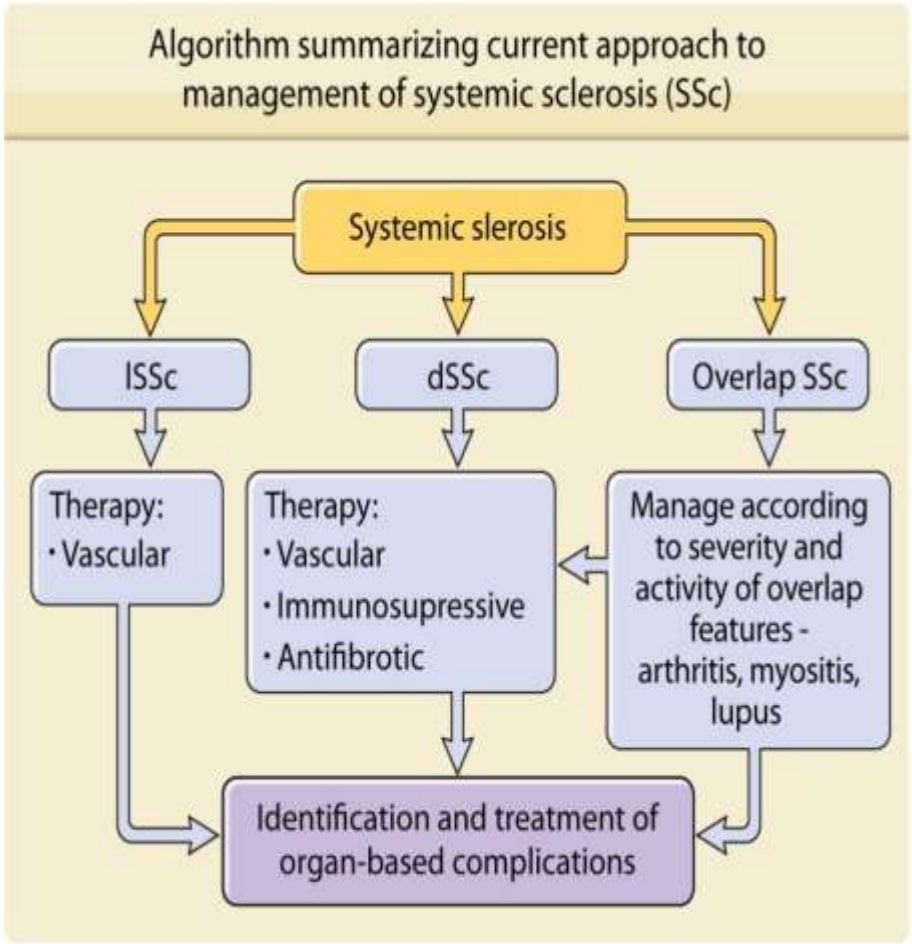
- Thrombocytopenia, rarely it can be as low as 20000/ cu.mm. It is often the first indicator of clinical improvement and occurs before fall in serum creatinine levels

Indicators of muscle involvement

- Elevated creatine phosphokinase levels
- excessive creatinuria
- Electromyography (EMG) is abnormal in 50% of patients who are early in the disease and in 93% in late stages
- MRI and spectroscopy are useful non-invasive methods to assess the disease activity

TREATMENT

The three basic pathologies of Systemic sclerosis are potentially amenable to therapeutic modulation, and this actually raises the possibility of true disease-modifying treatment. Presently vascular therapies and immunomodulation are the widely used candidate therapies. Antifibrotic treatment remains as a challenge and at present there is no proven antifibrotic agent.



Disease modifying treatments

Immunosuppressive agents that are effectively used for controlling connective tissue disorders generally have modest or no benefit in Systemic sclerosis.

Corticosteroids

When used in low doses, it reduces skin sclerosis, arthralgia, myalgia. Steroids do not retard the disease progression, nor does it induce the onset of renal crisis. There are case reports of Systemic sclerosis showing improvement with Dexamethasone pulse therapy[62].

Cyclophosphomide [63] has shown to retard the progressive of early ILD. Improvement in pulmonary function tests and HRCT is seen. It also produces a modest improvement in skin induration. Cyclophosphomide can be given daily orally or as intermittent intravenously. It is generally given at the dose 1-2 mg/kg/day for 6 – 12 months, although optimal duration of therapy is yet to be determined. Potential toxicities associated with the drug include bone marrow suppression, hemorrhagic cystitis, bladder carcinoma, premature ovarian failure, opportunistic infections.

Methotrexate shows moderate improvement in skin induration, its profibrotic effect leading to liver cirrhosis and ILD raises concern about using this drug.

Mycophenolate mofetil, azathioprine, cyclosporine, thalidomide, rapamycin, extracorporeal photophoresis have been reported to useful. Autologous stem cell transplantation is still in experimental stage.

Antifibrotic agents

D – penicillamine is antifibrotic, immunosuppressive agent, it prevents crosslinking of extracellular collagen fibers. It improves skin induration, prevents organ involvement and increases survival. Studies have shown that there is no difference in treatment outcome between standard dose 750 mg/day and very low dose 125mg alternate day [67].

Minocycline, INF γ , relaxin has failed to show improvement.

Treatment of Raynaud's phenomenon

Lifestyle modifications

- Protecting from environmental cold, especially in winters
- Using gloves and socks. Electrically heated gloves are now available.
- Avoiding use of cold water for washing
- Warming of hands in hot water for 5 – 10 minutes [65]
- Avoid smoking
- Avoid Beta blockers
- Avoiding use of vibratory tools

Pharmacological agents

Vasodilators –

1. Calcium channel blockers (CCB) - most commonly used and efficacious drugs. Nifedipine [64] 10 – 20 mg four times a day. calcium channel blockers relaxs the lower oesophageal sphincter and can exacerbate gastroesophageal reflux disease [66].
2. Angiotensin II receptor blockers (ARB) - effective and can be used alone or in combination with CCB.
3. α 1 adrenergic receptor blocker - Prazosin – 1mg three times a day
4. Ketanserin – 20 – 40 mg three times a day
5. Intravenous alprostadil (prostaglandin E_1) is used in refractory Raynaud's phenomenon
6. Oral iloprost
7. oral sildenafil has shown improvement in a study

Care should be taken so that the vasodilators do not excessively lower systemic blood pressure and diminish blood flow to the fingers.

Others

Low dose aspirin prevent platelet aggregation and is used as an adjuvant.

Pentoxifylline

Nerve block

Sympathectomy

Biofeedback

Treatment of skin sclerosis

As skin sclerosis is not life threatening and may regress spontaneously over a period of time, aggressive treatment for sclerosis is not advocated.

1. Low dose steroids – 5mg of Prednisolone is given for short courses. Steroids neither stops the progress of the disease nor induces renal crisis
2. D- penicillamine [67] - retrospective studies have shown considerable improvement in skin induration
3. Cyclophosphomide – modest improvement
4. Methotrexate – modest improvement

Moisturizing the skin and regular massaging of skin can be helpful.

Calcinosis cutis

Surgical removal

Carbondioxide Laser has superceded surgery

Low dose warfarin reduces inflammation around the calcium deposits

Nifedipine has been reported to be helpful

Telengiectasia

Can be removed for cosmetic purpose using Pulsed dye Laser

Treatment of Gastrointestinal complications

1. **Antireflux measures**

Lifestyle modifications

- Elevation of head end of the bed using pillows and blocks
- Heavy meals at noon, lighter meals at night.
- Taking frequent small meals.
- Avoiding food or liquids two hours before sleep.
- Quit smoking.
- Avoid spicy foods that increase acid production
- Nifedipine can relax lower esophageal sphincter resulting in reflux of food [66].

Specific treatment for Reflux

1. Drugs decreasing acid secretion – H 2 blockers, Proton Pump Inhibitors
2. Prokinetic drugs –These may be required in higher doses for treating reflux in scleroderma[3].

2 . watermelon stomach – recurrent bleeding can occur and can be treated by Laser photocoagulation

3. Malabsorption and malnutrition – rotational therapy using broad spectrum antibiotics like tetracycline, metronidazole, erythromycin to eradicate bacterial overgrowth. If malnutrition is severe, parentral hyperalimentation is indicated.
4. Octreotide injections are found helpful in chronic hypomotility present in Systemic sclerosis.

Treatment of respiratory complications

PAH

Continuous intravenous infusion of epoprostenol (prostacyclin) was the first line of management for pulmonary arterial hypertension in SSc patients. It is difficult to use as it is given in intensive care setup. Nowadays they used only in severe cases.

Most cases are treated with oral agents like

- Endothelin -1 receptor antagonists – bosentan, sitaxsentan [68]
- phosphodiesterase 5 inhibitor – sildenafil

If hypoxemia is present, oxygen supplementation should be given to prevent hypoxemia induce pulmonary vasoconstriction.

Inhaled delivery systems for iloprost have been introduced recently.

Lung transplantation is the last measure in patients who fail the above lines of management.

ILD

Cyclophosphomide has shown to retard the progress of early ILD. Improvement in pulmonary function tests and HRCT is seen. Cyclophosphomide can be given daily orally or as intermittent intravenously[63].

It is generally given at the dose 1-2 mg/kg/day for 6 – 12 months, although optimal duration of therapy is yet to be determined. Other drugs used are carbocysteine and low dose corticosteroid.

Renal crisis

Scleroderma renal crisis is a medical emergency, the outcome is mainly determined by the extent of renal damage at the time of initiation of treatment. Prompt recognition of early or impending scleroderma renal crisis is essential to avoid renal damage. Regular monitoring of blood pressure is advised. If the systolic blood pressure increases by 20 mmHg or the diastolic blood pressure increases by 10 mmHg from the baseline values, renal crisis should be suspected. Treatment is with ACE inhibitors is crucial. With the use of ACE inhibitors in SRC, the mortality have come down [45]. Non Steroidal Anti Inflammatory Drugs (NSAID) and glucocorticoids should be avoided. Short term dialysis is done and after recovery dialysis is discontinued. If the patient is unable to discontinue dialysis even after 1 – 2 years renal transplantation should be considered.

AIM OF THE STUDY

1. To study the epidemiological features of Systemic sclerosis with respect to incidence, age of onset, sex.
2. To study the occupational risk factors for Systemic sclerosis.
3. To study the skin manifestations of Systemic sclerosis.
4. To study the systemic manifestations of Systemic sclerosis.

MATERIALS AND METHODS

This study was conducted in the Department of Dermatology, Government Rajaji Hospital, Madurai during the period of september 2012 to August 2014 (24 months)

INCLUSION CRITERIA:

All consenting patients fulfilling ARA criteria for systemic sclerosis

- major criterion - Scleroderma proximal to digits, affecting limbs, face, neck or trunk

  or

- two minor criteria -

  (a) sclerodactyly

  (b) digital pitted scarring

  (c) bilateral basal pulmonary fibrosis

EXCLUSION CRITERIA:

1) Patients not consenting for examination
2) Patients not fulfilling ARA criteria for systemic sclerosis

All the patients attending the outpatient department of Dermatology, Government Rajaji Hospital were screened during the study period between September 2012 and August 2014 and patients satisfying the above mentioned criteria were enrolled in the study. After getting their informed consent, a detailed history was taken and a thorough dermatological and systemic examination was done.

The parameters studied were the age of onset, duration of disease, sex ratio, occupation, duration of exposure to harmful environmental factors, presenting complaint, extent of skin involvement, presence of sclerodactyly, fingertip ulcer, stellate scars, gangrene, digit loss, scleroderma facies, Raynaud's phenomenon, neck sign, round finger pad sign, calcinosis cutis, pigmentary changes, nail involvement, loss of hair in the extremities, hypohidrosis, leg ulcer, associated skin diseases. Systemic involvement was evaluated clinically and investigations including complete blood count, ESR, renal function tests, blood sugar, liver function tests, urine routine were done for all the cases. X-ray chest PA view, HRCT – chest, Pulmonary function test, ultrasound of abdomen and pelvis, ECG, ECHO, Barium Swallow, upper GI scopy, X ray of both hands were done for all the cases. In selected cases EMG, muscle biopsy, skin biopsy, DIF, ANA, Scl 70, U1RNP, and dsDNA was done. All the data was further compiled and inferences were drawn.

OBSERVATIONS AND RESULTS

In this study, 20 cases of Systemic sclerosis were enrolled in the Department of Dermatology, Government Rajaji Hospital, Madurai, during a study period of two years. The following observations were noted.

INCIDENCE

The total number of patients who attended the Dermatology out patient department during the study period was 100814. The number of patients diagnosed with Systemic sclerosis were 20, so the overall incidence of Systemic sclerosis was found to be 0.2 per dermatology cases.

TABLE 1 – INCIDENCE OF SYSTEMIC SCLEROSIS

Total no of patients attending Dermatology OP	100814
Patients diagnosed with Systemic sclerosis	20
Incidence per 1000 cases	0.2

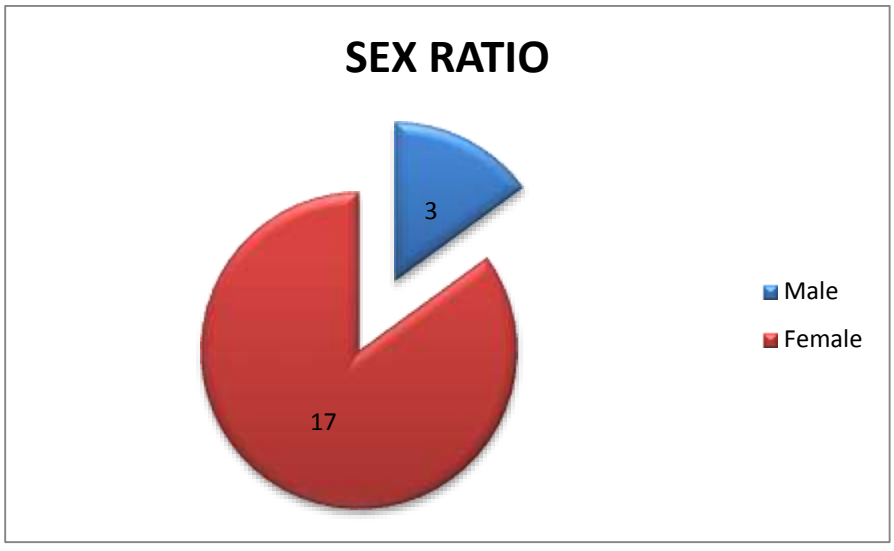
SEX RATIO

In our study, out of 20 cases, 3 cases (15 %) were males and 17 (85%) cases were females. The female: male ratio was 5.67 : 1 (Table 2, figure 1)

TABLE 2- SEX RATIO

GENDER	NO. OF CASES
Male	3
Female	17

FIGURE 1 – SEX RATIO



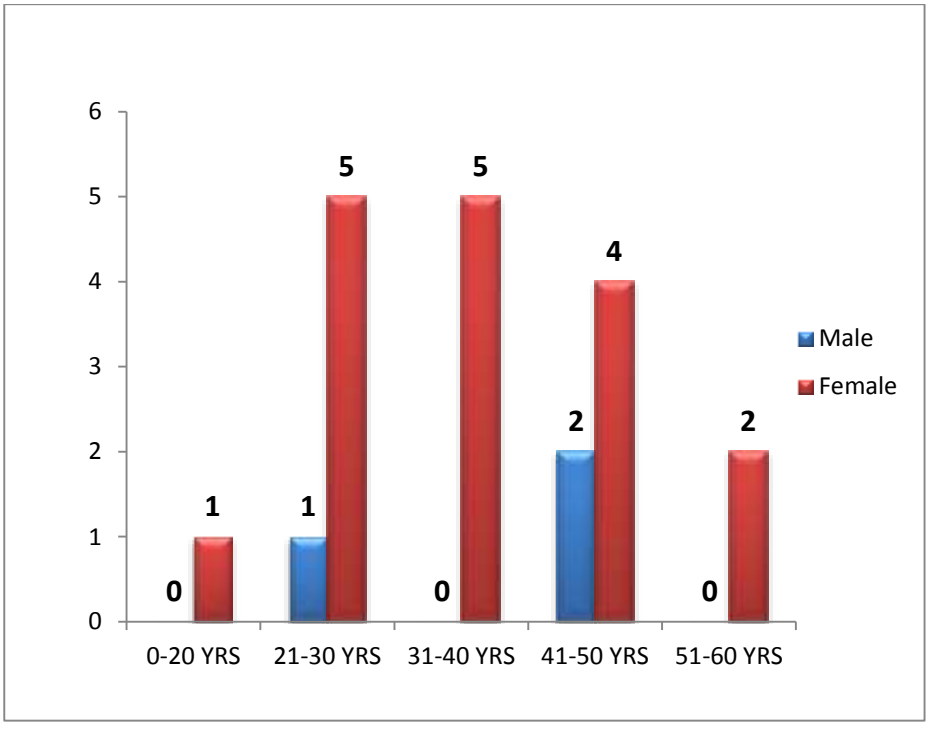
AGE OF ONSET

In our study the minimum age of onset of the disease was 10 years whereas the maximum age reported was 53 years. Most of the patients were between the ages of 21 - 50 years when the disease started . Mean age of onset was 36 yrs. (Table 3, figure 2)

TABLE 3 - AGE OF ONSET

Age interval	Male	Female	Total	percentage
0-20	0	1	1	5%
21-30	1	5	6	30%
31-40	0	5	5	25%
41-50	2	4	6	30%
51-60	0	2	2	10%

FIGURE 2 - AGE OF ONSET



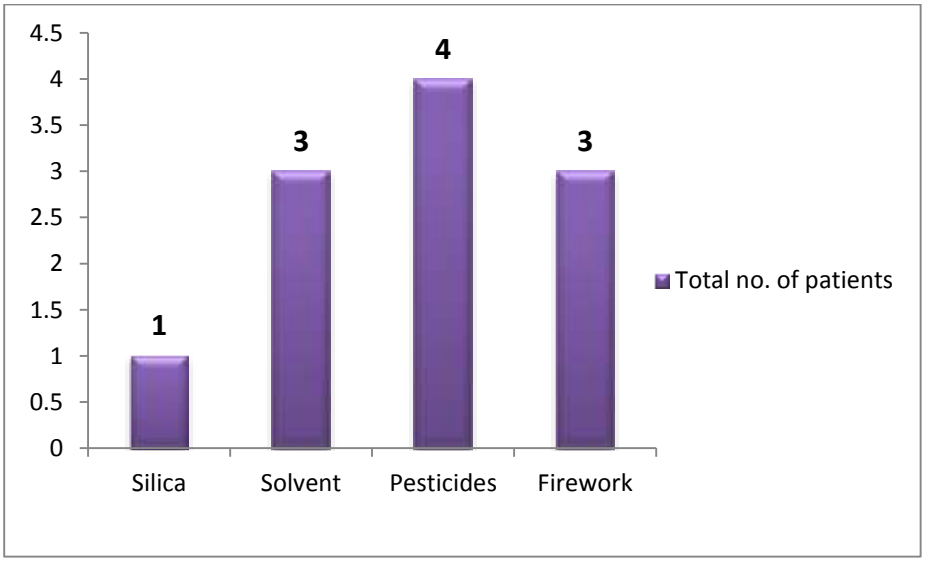
OCCUPATION – EXPOSURE TO ENVIRONMENTAL FACTORS

Exposure to environmental factors which can contribute to the pathogenesis was present in 11 patients. Pesticides, solvents, firework were commonly involved. Exposure to silica was seen in one patient. (Table 4, figure 3)

TABLE 4 - EXPOSURE TO ENVIRONMENTAL FACTORS

Exposure	Males	Females	Total no. of patients	Percentage
Nil	1	8	9	45%
Silica	1	0	1	5%
Solvent	1	2	3	15%
Pesticides	0	4	4	20%
Firework	0	3	3	15%

FIGURE 3 – EXPOSURE TO ENVIRONMENTAL FACTORS



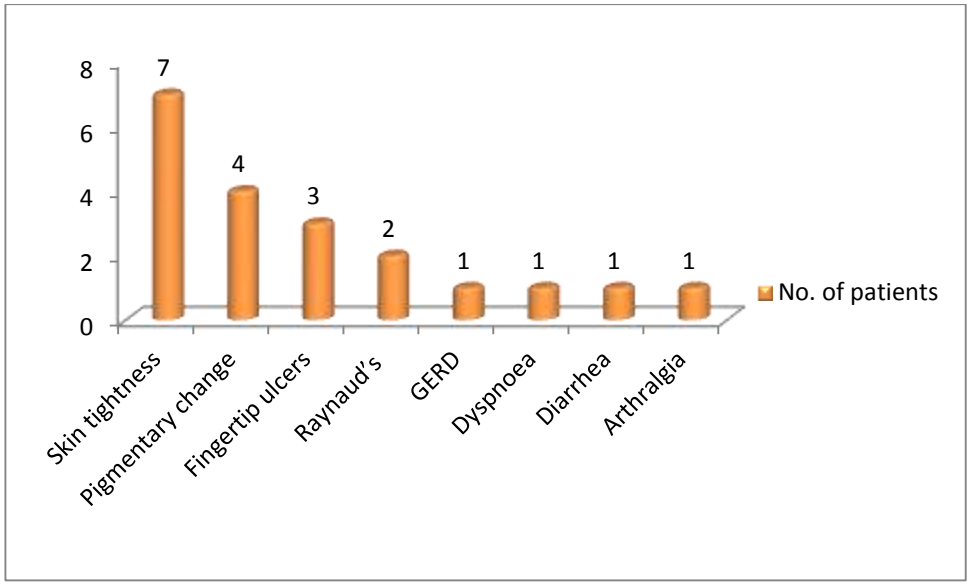
PRESENTING COMPLAINT

The most common presenting complaint was tightness of skin which was in about 35 % of cases. (Table 5, figure 4)

TABLE 5 - PRESENTING COMPLAINT

Presenting complaint	No. of patients	Percentage
Skin tightness	7	35%
Pigmentary change	4	20%
Fingertip ulcers	3	15%
Raynaud's phenomenon	2	10%
GERD	1	5%
Dyspnoea	1	5%
Diarrhea	1	5%
Arthralgia	1	5%

FIGURE 4 – PRESENTING COMPLAINT



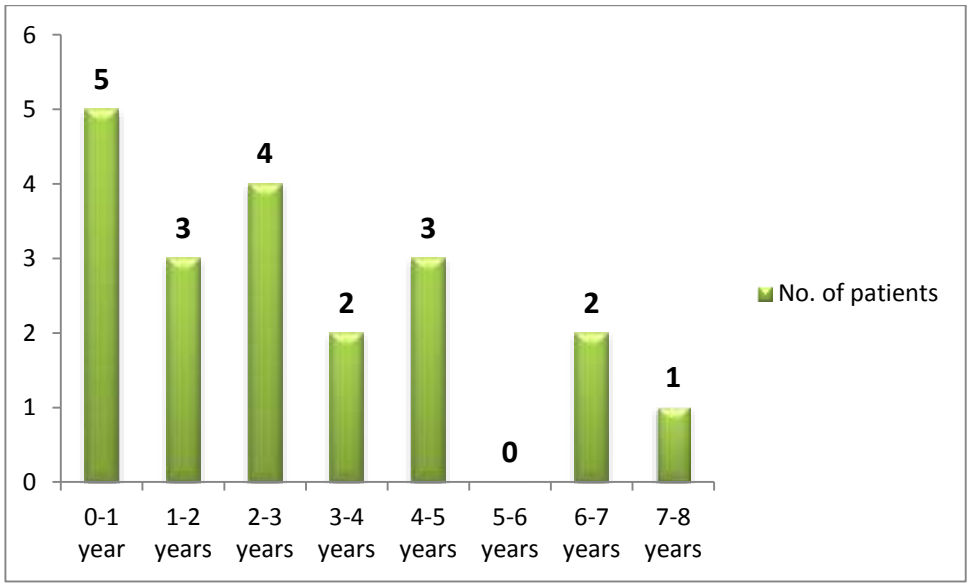
DURATION OF ILLNESS

Most patients presented within 2 years of onset of disease. Only 3 patients waited for more than 6 years to seek medical help. Mean duration of illness is 3.3 years.(Table 6, figure 5)

TABLE 6- DURATION OF ILLNESS

Duration	No. of patients	Percentage
0-1 year	5	25%
1-2 years	3	15%
2-3 years	4	20%
3-4 years	2	10%
4-5 years	3	15%
5-6 years	0	0%
6-7 years	2	10%
7-8 years	1	5%

FIGURE 5 – DURATION OF ILLNESS



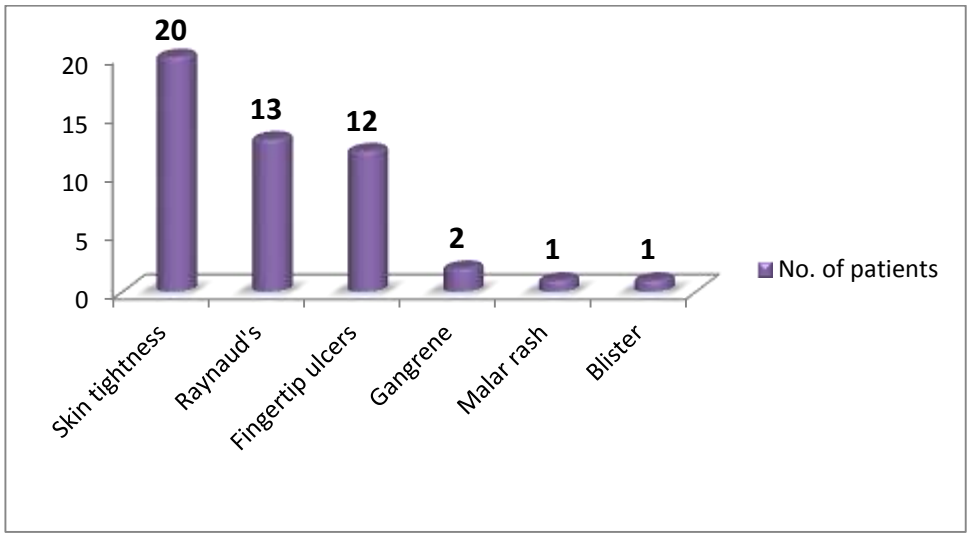
SKIN INVOLVEMENT

Skin tightness was present in all 20 patients, Raynaud's phenomenon was noted in 13 patients, fingertip ulcers in 12 patients. Two patients had gangrene. One patient had malar rash and one had blisters in leg (Table 7, figure 6)

TABLE 7 - SKIN INVOLVEMENT

History	No. of patients	Percentage
Skin tightness	20	100%
Raynaud's phenomenon	13	65%
Fingertip ulcers	12	60%
Gangrene	2	10%
Malar rash	1	5%
Blister	1	5%

FIGURE 6 – SKIN INVOLVEMENT



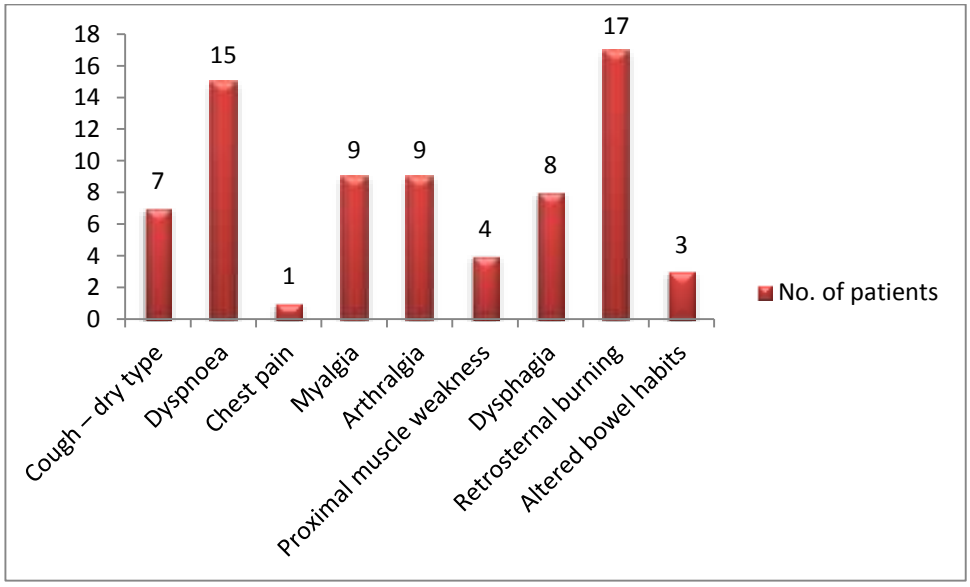
SYSTEMIC INVOLVEMENT

Most common systemic complaint was retrosternal burning, next common being dyspnoea. All complaints relating to systemic involvement are enumerated in Table 8, figure 7

TABLE 8 - SYSTEMIC INVOLVEMENT

History	No. of patients	Percentage
Cough – dry type	7	35%
Dyspnoea	15	75%
Chest pain	1	5%
Myalgia	9	45%
Arthralgia	9	45%
Proximal muscle weakness	4	20%
Dysphagia	8	40%
Retrosternal burning/ regurgitation	17	85%
Altered bowel habits	3	15%
GI bleeding	0	0%

FIGURE 7- SYSTEMIC INVOVEMENT



EXTENT OF SKIN SCLEROSIS

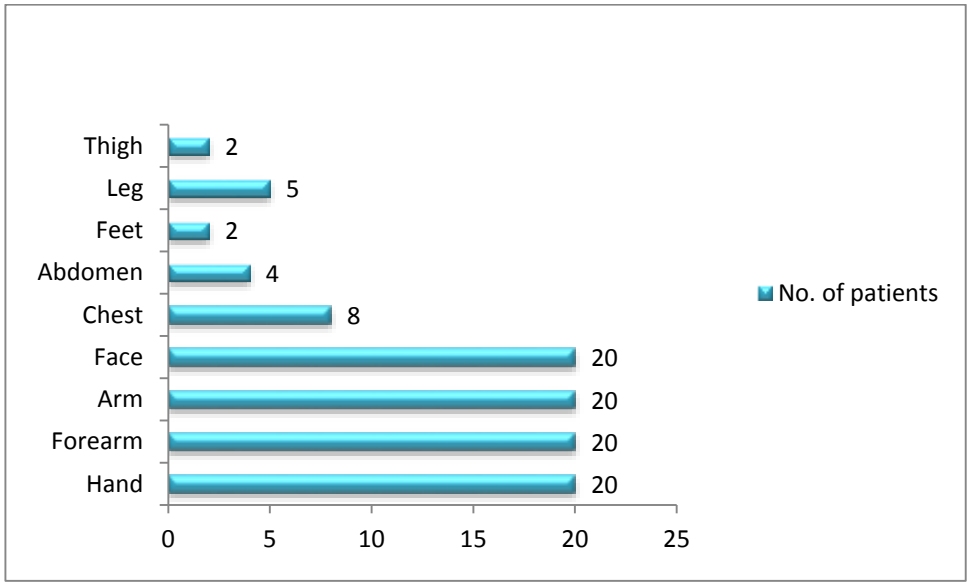
Skin tightness of hand, forearm, arm and face was seen in all patients.

Lower limb was less frequently involved (Table 9, figure 8)

TABLE 9 - EXTENT OF SKIN SCLEROSIS

Site	No. of patients	Percentage
Hand	20	100%
Forearm	20	95%
Arm	20	85%
Face	20	100%
Chest	8	40%
Abdomen	4	20%
Feet	2	10%
Leg	5	25%
Thigh	2	10%

FIGURE 8 – EXTENT OF SKIN SCLEROSIS



MODIFIED RODNAN SCORE

Modified Rodnan Skin Score was measured at 17 sites. Minimum score was 13 and maximum was 37. Mean score was 18.

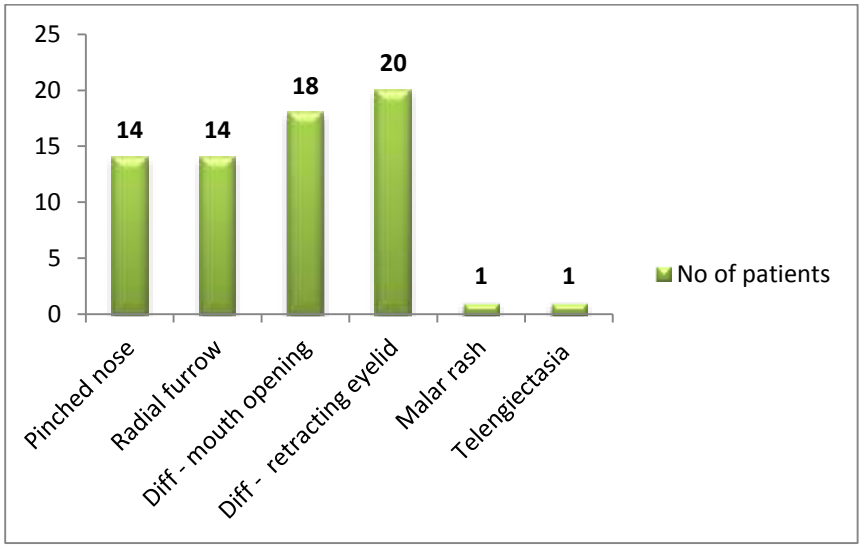
SKIN CHANGES IN FACE

Difficulty in retracting the lower eyelid was seen in all patients. Difficulty in opening the mouth was present in 18 cases. Pinched nose and fish mouth appearance were seen 14 patients. One had telengiectasia in the cheeks.

(Table 10, figure 9) TABLE 10 - SKIN CHANGES IN FACE

Skin change	No of patients	Percentage
Pinched nose	14	70%
Radial furrow/ fish mouth	14	70%
Difficulty in mouth opening	18	90%
Difficulty in retraction of lower eyelid	20	100%
Malar rash	1	5%
Telengiectasia	1	5%

FIGURE 9 – SKIN CHANGES IN FACE



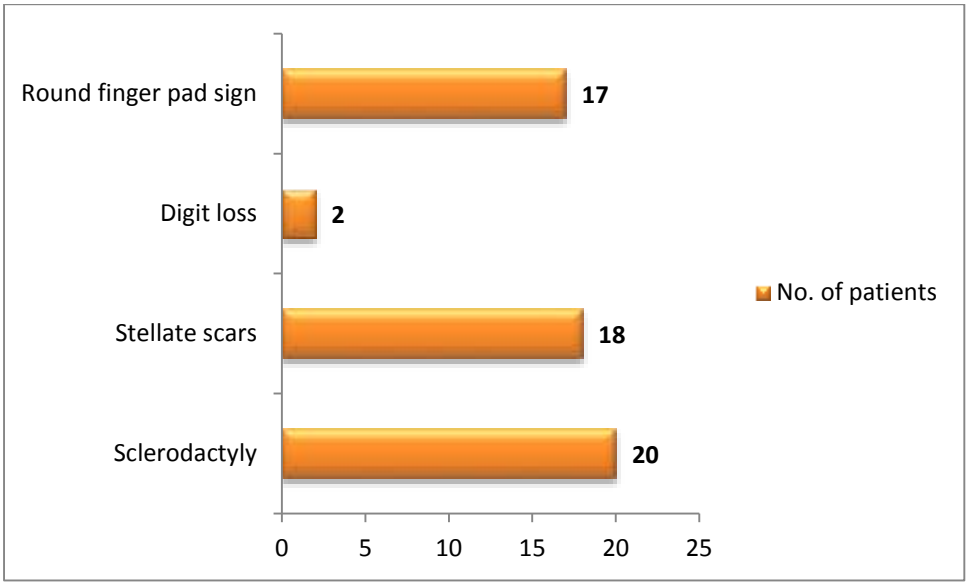
SKIN CHANGES IN HAND

All 20 patients had sclerodactyly. Stellate scars were present in 18 patients and round finger pad sign in 17 patients. Two patients had loss of digits. (Table 11, figure 10)

TABLE 11 - SKIN CHANGES IN HAND

Skin changes	No. of patients	Percentage
Sclerodactyly	20	100%
Stellate scars	18	90%
Digit loss	2	10%
Round finger pad sign	17	85%

FIGURE 10 – SKIN CHANGES IN HAND



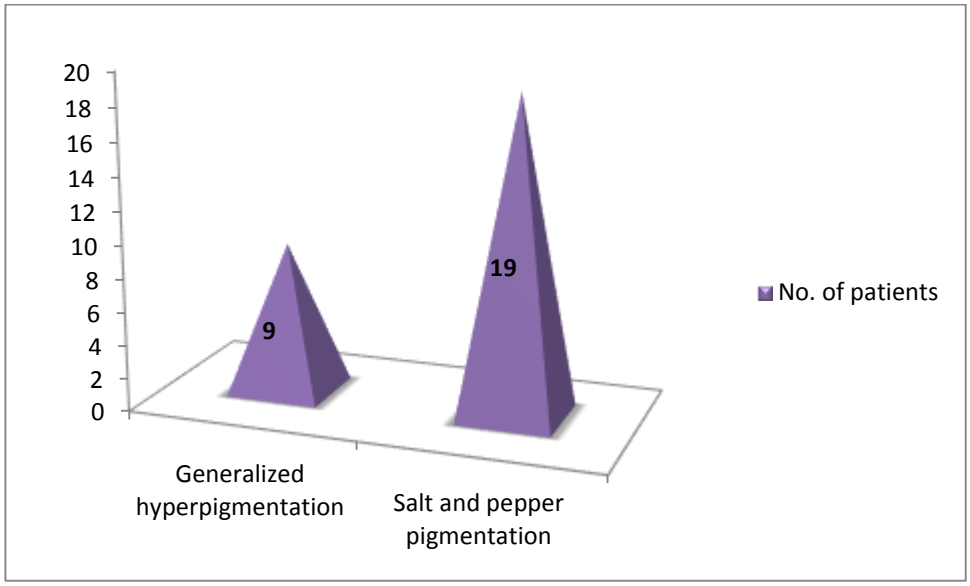
CHANGES IN PIGMENTATION

Generalised hyperpigmentation was seen in 9 patients. Salt and pepper pigmentation was present in 19 patients.(Table 12, figure 11)

TABLE 12 - CHANGES IN PIGMENTATION

Skin change	No. of patients	Percentage
Generalized hyperpigmentation	9	45%
Salt and pepper pigmentation	19	95%

FIGURE 11 – CHANGES IN PIGMENTATION



OTHER SKIN CHANGES

Calcinosis cutis was present in two patients. Neck sign was seen in 16 patients. Loss of hair in the extremities was seen in 10 patients and hypohidrosis in 13 patients. One patient had leg ulcer.

TABLE 13 - OTHER SKIN CHANGES

Skin change	No. of patients	Percentage
Calcinosis cutis	2	10%
Neck sign	16	80%
Leg ulcer	1	5%
Loss of hair – extremities	10	50%
Hypohidrosis	13	65%

NAIL INVOLVEMENT

Most common nail change was ragged cuticle and was seen in 11 patients. Two had racquet nails and one had longitudinal melanonychia (Table 14)

TABLE 14 NAIL INVOLVEMENT

Nail change	No. of patients	Percentage
Ragged cuticle	11	55%
Racquet nail	2	10%
Longitudinal melanonychia	1	5%

Evaluation of blistering disorder

One patient had multiple, tense vesicles of both upper and lower limb.

It was associated with intense itching.

Oral erosions were present

Nikolsky – negative

Bulla spreading sign – positive

Tzanck smear showed eosinophils and acantholytic cells were absent.

Biopsy showed normal epidermis, increased collagenisation of the dermis, subepidermal bulla.

DIF showed linear and granular deposits of IgG, IgM, IgA, fibrin, C3 along basal layer.

Salt split technique showed IgA and C3 along the dermal side of the split.

ANA - positive

Scl 70 - positive

dsDNA - negative

patient did not fulfill the ARA criteria for SLE

All these features were suggestive of Epidermolysis bullosa Acquisita

EXAMINATION OF RESPIRATORY SYSTEM

On auscultation, crepitations were present in basal lung fields in 8 patients. Chest expansion was decreased in 18 patients (Table 15)

TABLE 15 - EXAMINATION OF RESPIRATORY SYSTEM

Findings	No. of patients	Percentage
Auscultation - crepitations	8	40%
Decreased chest expansion	18	90%

MUSCLE INVOLVEMENT

Proximal muscle weakness was present in four patients but tenderness was seen in one patient. In this patient EMG showed low amplitude, slow wave, polyphasic fibrillation. Muscle biopsy was done and it showed cross and longitudinal section of muscle bundle with intervening fibrosis and fatty tissue. Focal area show degenerating and regenerating muscle fibres with inflammatory cell infiltrate, suggestive of myositis.

ASSOCIATED CONDITIONS

Common dermatological diseases like psoriasis, dermatophytosis, tinea versicolor, plantar wart were seen in few Systemic sclerosis patients. Two patients had hypothyroidism (Table 16)

TABLE 16 - ASSOCIATED CONDITIONS

Condition	No of patients	Percentage
Psoriasis	1	5%
Dermatophytosis	2	10%
Tinea versicolor	1	5%
Plantar wart	1	5%
Hypothyroidism	2	10%

COMPLETE BLOOD COUNT

Anaemia was present in 5 patients. ESR was elevated in (Table 17)

TABLE 17 - COMPLETE BLOOD COUNT

CBC	No. of patients	Percentage
Anaemia	5	25%
Elevated ESR	14	70%

RFT/LFT

All 20 patients had normal renal and liver function test

Urine Routine

Urine routine was within normal limits in all 20 patients. No patient had proteinuria

IMAGING STUDIES FOR LUNG INVOLVEMENT

For detecting lung involvement both Chest X ray PA view and HRCT – chest were done. Features of Interstitial Lung Disease was seen in 12 patients's chest Xray and 19 patients's HRCT. (Table 18)

TABLE 18 - IMAGING STUDIES FOR LUNG INVOLVEMENT

Test	No. of patients having ILD	Percentage
Chest Xray PA view	12	60%
HRCT – chest	19	95%

PULMONARY FUNCTION TEST

Pulmonary function test showed normal spirometry in one patient. In rest 19 patients restrictive type was noted of which 4 had mild restriction and 15 had moderate restriction.(Table 19)

TABLE 19 - PULMONARY FUNCTION TEST

Pattern	No.of patients	Percentage
Normal	1	5%
Mild restriction	4	20%
Moderate restriction	15	75%
Severe restriction	0	0%

ECG

Electrocardiography was within normal limits in 19 patients. One patient had low voltage QRS complex (Table 20)

TABLE 20 - ECG CHANGES

ECG changes	No. of patients	Percentage
Within normal limits	19	95%
Low voltage QRS complex	1	5%

ECHO CARDIOGRAM

In this study, ECHO Cardiogram was found to be normal in 19 patients. Pulmonary Arterial Hypertension was present in one patient. (Table 21)

TABLE 21 – ECHO CARDIOGRAM

ECHO	No. of patients	Percentage
Normal	19	95%
Pulmonary Arterial Hypertension	1	5%

BARIUM SWALLOW

Barium swallow done showed normal motility in 18 patients, dysmotility in 1 patient and narrowing of thoracic oesophagus in 1 patient. (Table 22)

TABLE 22 - BARIUM SWALLOW

Finding	No. of patients	Percentage
Normal	18	90%
Dysmotility	1	5%
Narrowing of thoracic oesophagus	1	5%

UPPER GI SCOPY

Upper GI scopy was done for all 20 patients, it was normal in 11 patients. Oesophagitis was present in 8 patients and lax gastroesophageal sphincter was present in one patient.(Table 23)

TABLE 23 - UPPER GI SCOPY

Finding	No. of patients	Percentage
Normal	11	55%
Oesophagitis	8	40%
Lax sphincter	1	5%

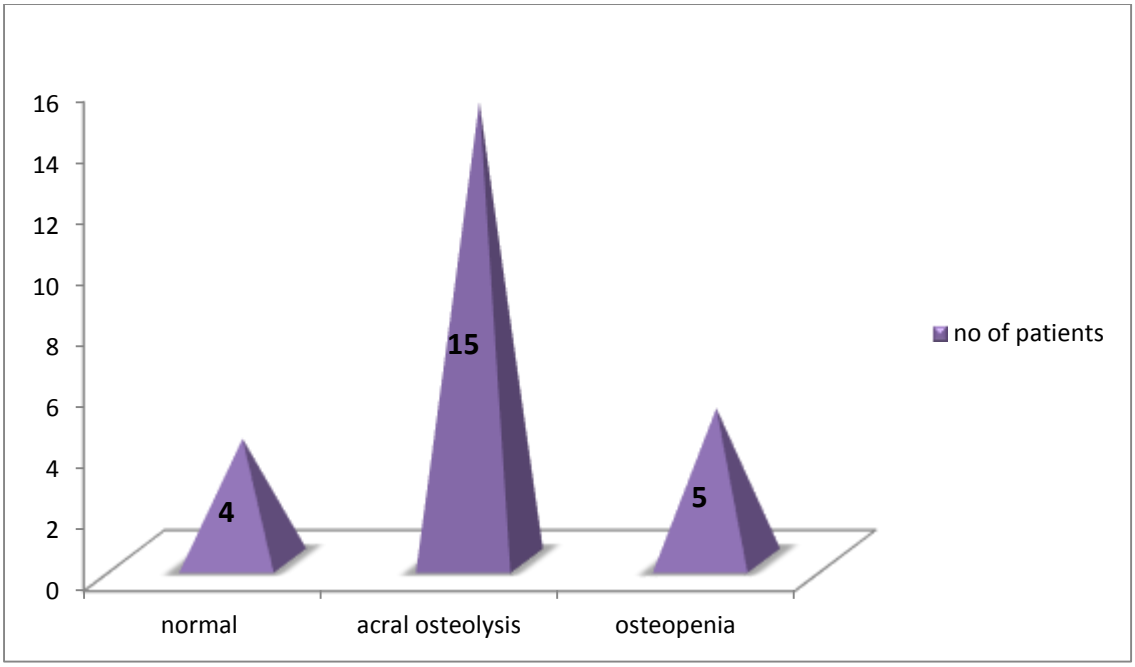
X RAY OF HANDS

Xray of hands showed acral osteolysis in 15 patients and osteopenia in 5 patients. It was normal in 4 patients. (Table 24, figure 12)

TABLE 24 - X RAY OF HANDS

Finding	No. of patients	Percentage
Normal	4	20%
Acral osteolysis	15	75%
osteopenia	5	25%

FIGURE 12 – X RAY OF HANDS



ULTRASOUND ABDOMEN

Ultrasonography of abdomen and pelvis was normal in 17 patients. Two patients had renal calculi and one had increased renal cortical echoes. (Table 25)

TABLE 25 - ULTRASOUND ABDOMEN

Finding	No. of patients	Percentage
Nil	17	85%
Renal calculi	2	10%
Increased renal cortical echoes	1	5%

DISCUSSION

We enrolled 20 cases of Systemic sclerosis in this study which was done over a span of two years.

INCIDENCE

Out of a total of 100814 cases visiting the dermatology out-patient department during the study period the cases with Systemic sclerosis were 20. Thus the incidence rate of Systemic sclerosis was 0.2 per dermatology cases.

Incidence of the disease show a wide variation in the studies conducted so far. The incidence of Systemic sclerosis in US is 20 per million population. In a study conducted by Giersson et al[75] in Iceland, the incidence was 3.8 per million population. Roberts- Thomson et al[76] found the incidence to be 15 per million in their study in Australia. Epidemiological data from India is lacking.

SEX RATIO

In our study the male to female ratio was 1: 5.7, showing a female preponderance. This is similar to the previous studies. In a study done in North India by Sharma VK et al[74] the ratio was 1 : 5.2.

Roberts- Thomson et al[76] found the ratio to be 1:5 in Australia. In Afro Caribbean population, Flower et al[73] observed the ratio to be 1:4.6

AGE OF ONSET

The youngest patient reported to have Systemic sclerosis in our study was of age 10 years and the maximum age reported was 53 years.

Patients were most commonly in the third, fourth and fifth decade. 95% of patients were in the age group 21- 60 years. Similarly Ghosh et al[81], in Eastern India found that 85 % of patients were in the age group 21- 60 years.

In our study, the mean age of onset was 36 years. This is comparable with the previous studies from India. In the north Indian study conducted by SharmaVK et al[74] the mean age of onset was 32.75 years. In Eastern India, Ghosh et al[81] found the mean age of onset to be 29.6 years.

OCCUPATION – EXPOSURE TO ENVIRONMENTAL FACTORS

Environmental factors can contribute to the pathogenesis. Exposure to such substances were present in 11 patients (55%). Solvents (15%), pesticides(20%) , firework (15%) were commonly involved. Exposure to silica was seen in one patient.

Diot, Lesire, Guilmot, et al[77] in their case control study had shown significant association with occupational risk factors like silica, solvents, epoxy resins.

PRESENTING COMPLAINT

In our study, the most common presenting complaint was skin tightness, seen in about 35%. Eventhough tightness was present in all 20 cases at the time of presentation it was the concern of the patient only in 35%. Similarly pigmentary change was present in 95%, but it was the presenting complaint in only 20%. Other presenting complaints include fingertip ulcers, Raynaud's phenomenon, GERD, dyspnoea, diarrhea, arthralgia.

DURATION OF ILLNESS

In our study Duration of illness varied between 4 months to 8 yrs and the mean duration of illness was 3.3 years.

In the study done by Sharma VK et al[74], the mean duration was 6.75 years. Reveille JD et al[71] reported the duration as 2.5 years in Hispanics, 2 years in African Americans and 1.7 years in Americans presenting to Rheumatology clinic. Ghosh et al[81] in his study done in Eastern India reported the duration as 23 months.

SKIN INVOLVEMENT

Most common involvement of skin was tightness of skin which was present in all cases (100%). Next common were Raynaud's phenomenon (13 cases – 65%) and fingertip ulcers (12 cases – 60%).

Raynaud's phenomenon was found in more number of patients in studies done by Sharma et al[74] in North India (92.9%) , Ruangjutipopan et al[70] in Thailand (94.1%) and Al Adhadh et al[72] in Saudi Arabia (100%). Low percentage in our study is probably because of higher temperature throughout the year in South India.

Fingertip ulcers were present in 58.6%, 53.6% and 47.4% in the studies done by Sharma et al[74], Ruangjutipopan et al[70], Krishnamurthy et al[69] respectively. This is comparable to the observation made in our study.

Gangrene was present in two cases (10%), this is similar to the study done by Sharma et al[74] (6.7%).

SYSTEMIC INVOLVEMENT

In our study, Retrosternal burning sensation and regurgitation was present in 17 patients (85%). This was similar to the studies done in US by Flower et al[73] and Reveille JD et al[71].

Dysphagia was present in 8 patients (40%) and altered bowel habits was present in 3 cases (15%). Of the three patients two had diarrhea and one had constipation. Similarly, dysphagia was present in 35.2 % in the study done by Sharma et al[74] and in 41.2 % in the study done by Ruangjutipopan et al[70] in Thailand. Whereas in Al Adhadh et al[72] recorded a higher incidence of 87% in Saudi Arabia.

In our study, 15 patients (75%) had breathlessness and 7 (35%) out of them had dry cough. This was higher than the previous studies done by Sharma et al [74](51.1%), Al Adhadh et al[72](57.4%), Krishnamurthy et al[69](19.2%).

One patient (5%) had chest pain, when evaluated was found to have pulmonary arterial hypertension.

Myalgia and arthralgia were present in 9 cases (45%). This was similar to the studies done by Sharma et al[74] (36.7%) and Ruangjutipopan et al[70] (52.3%), whereas it was higher in studies done by Krishnamurthy et al[69] (66.7%) and Al Adhadh et al[72](96 %).

Proximal muscle weakness was present in 4 cases. Of which one patient had severe muscle tenderness, elevated muscle enzymes, EMG and muscle biopsy suggestive of myositis. She also had malar rash. ANA was positive. U1RNP was positive. This patient was a case of overlap syndrome – Systemic sclerosis, SLE and Dermatomyositis – Mixed connective tissue disease.

EXTENT OF SKIN SCLEROSIS

In our study, most common sites involved were hand, forearm, arm and face, which was present in all 20 cases (100%). Involvement of chest in 40 % , abdomen in 20 %. Lower limb was the least common site. Involvement in legs 25%, thigh and feet in 10 %. This is similar to previous studies done, Sharma VK et al[74] reported skin sclerosis in 98.5%, Krishnamurthy V et al[69] in 100%, Al Adhadh et al[72] in 96.5%.

In our study, Modified Rodnan skin score varied between 13 and 37, mean score being 18. This is similar to the study done by Reveille JD et al[71] in US where the score was 14 in whites , 15 in Hispanics and 16 in African Americans. But it is low compared to a study done in North India done by Sharma et al[74] where the score was 25.81. The variation in the score is due to the difference in the stage in which the patients were examined.

SKIN CHANGES IN FACE

In our study, 14 patients (70%) had pinched nose and fish mouth appearance and 18 patients (90%) had difficulty in opening the mouth.

In all 20 patients difficulty in retracting the lower eyelid was present. One patient had malar rash and one had telengiectsia.

Similar to our study, difficulty in mouth opening was present in 82.6%, in the study by Ghosh et al[81]. But in the study by Sharma et al[74] difficulty in mouth opening was present only in 55.5%.

Telengiectasia was present only in one patient (5%) in our study. But higher incidence of telengietasia have been reported by Flower et al[73] in Afro Caribbean as 48%, Sharma et al[74] in North India as 36.8% and Ghosh et al[81] in East India as 23.1%.

SKIN CHANGES IN HAND

In our study, sclerodactyly was present in all 20 patients (100%), similar to the study done by Ghosh et al[81] in East India where it was present in 82.6%.

Stellate scars in digits were present noted in 18 (90%) patients, which was a little higher compared to the previous studies done by Ghosh et al[81] (63%) and Flower et al[73] (70%).

Round finger pad sign was present in 17 (85%) patients whereas Mizutani et al[31] described in 100 % patients. In all 13 patients who had Raynaud's phenomenon, Round finger pad sign was present.

Round finger pad sign was present in 4 cases who did not have Raynaud's phenomenon. These 4 patients had fingertip scars. This is could be due to vascular involvement, in the absence or subclinical Raynaud's phenomenon leading to loss of pulp tissue.

Two patients (10%) had loss of digits due to gangrene. This is similar to studies done by Sharma et al[74] (6.7%) and Ghosh et al[81] (6.5%)

CHANGE IN PIGMENTATION

Salt and pepper pigmentation was present in 19 (95%) patients. This is relatively high when compared to studies done by Sharma et al[74] (51.2%) and Ghosh et al[81] (54.3%).

Generalized hyperpigmentation was noted in 9 (45%) patients. Similar occurrence was noted in the study done by Ghosh et al[81] (36.9%). Whereas Sharma et al[74] recorded 88.1% patients with diffuse hyperpigmentation.

OTHER SKIN CHANGES

In our study, neck sign was positive in 16 (80%) patients. This is similar to the report by Barnett A.J. [32]who initially recorded neck sign in 90%. Ghosh et al[81] recorded calcinosis cutis in 2.2 % and Flower et al[73] in 11%, similarly in our study calcinosis cutis was present in 5%.

Loss of hair in extremities was noted in 10 (50%) patients. Hypohidrosis was seen in 13 (65%) patients. One patient had leg ulcer.

One patient had multiple, tense vesicles of both upper and lower limb. It was associated with itching. Nikolsky – negative, bulla spreading sign – positive. She also had oral erosions. With clinical findings, a differential diagnosis of lymphangiectatic blister due to sclerosis, associated autoimmune blistering disorders like bullous SLE, Epidermolysis bullosa Acquisita were considered.

Tzanck smear showed eosinophils and acantholytic cells were absent. Biopsy showed normal epidermis, increased collagenisation of the dermis, subepidermal bulla. DIF was done, it showed linear and granular deposits of IgG, IgM, IgA, fibrin, C3 along basal layer. Salt split technique showed IgA and C3 along the dermal side.

ANA and Scl 70 were positive but dsDNA was negative. There was no other clinical feature of SLE, ARA criteria was not fulfilled. With these findings a diagnosis of Epidermolysis bullosa Acquisita was made.

NAIL INVOLVEMENT

Ragged cuticle was seen in 11 (55%) patients. Other nail changes present were racquet nail (10%) and longitudinal melanonychia(5%). Elmansour et al[78] recorded ragged cuticle in 37.5% patients and longitudinal melanonychia in 12.5%.

ASSOCIATED CONDITIONS

Few other skin conditions were observed in Systemic sclerosis patients. A single case each of psoriasis, tinea versicolor, plantar wart and two cases of dermatophytosis were noted. Two patients had hypothyroidism. One patient had overlap with connective tissue diseases SLE and dermatomyositis.

COMPLETE BLOOD COUNT

Anaemia was recorded in 5 (25%) patients and elevated ESR was recorded in 14 (70%) patients in our study. In our study, ESR values did not correlate with the severity of the disease. Elevated ESR was also seen in the studies by Sharma et al[74] (87.8%) and Krishnamurthy et al[69] (70.5%).

RFT & LFT

All 20 patients had normal liver and renal function test.

Urine routine was normal in all patients, no patient had proteinuria.

No patient in the study had renal involvement. This was the same in the study by Krishnamurthy et al[69] done in South India. Similarly Sharma et al[74] recorded proteinuria in 6% patients in north India. This is strikingly low when compared to western literature where Cannon et al[79] recorded proteinuria in 36%, abnormal RFT in 19% patients. Palma A et al[80] also recorded abnormal parameters in 45% patients.

RESPIRATORY SYSTEM

On examination, 18 (90%) patients had decreased chest expansion and crepts were heard in the basal lung fields in 8 (40%) patients.

In our study, Interstitial lung disease was present in 19 (95%) patients. Diagnosis was made by HRCT chest. Of these 19 patients, only in 12 patients Chest X ray showed lung involvement. This is higher compared to studies done by Sharma et al[74] (65%), Flower et al[73] (30%), Krishnamurthy et al[69] (21.8%)

Pulmonary function test showed mild restrictive pattern in 4 (20%) patients and moderate restrictive pattern in 15 (75%) patients.

CARDIOVASCULAR SYSTEM

ECG was within normal limits in 19 patients. One patient had low voltage QRS complex, on subsequent ECHO cardiogram, no abnormality was found.

ECHO showed pulmonary arterial hypertension in one (5%) patient. This is similar to studies done by Flower et al[73] and Reveille JD et al[71].

GASTROINTESTINAL SYSTEM

Upper GI scopy showed oesophagitis in 8 (40%) patients and lax gastroesophageal sphincter in one (5%) patient.

Barium swallow study showed dymotility in one (5%) patient and narrowing of thoracic oesophagus in one (5%) patient. Study done in South India by Krishnamurthy et al[69] showed 20.4%, similar to our study. A higher incidence of abnormalities have been recorded in studies done by Sharma et al[74] (70.2%), Reveille JD et al[71] (70%)

X RAY OF HANDS

In our study, X ray of hands showed acral osteolysis in 15 (75%) patients and osteopenia in 5 (25%) patients. Results were comparable to the study done by Sharma VK et al[74] where acral osteolysis was present in 58.3% and osteopenia in 19.4%.

Out of the 13 patients who had Raynaud's phenomenon, 11(84.6%) had acral osteolysis. Out of the 18 patients with fingertip scars, 15 (83.3%) had acral osteolysis. Hence acral osteolysis correlates with Raynaud's phenomenon and fingertip scars.

ULTRASOUND ABDOMEN

Ultrasound abdomen was normal in 17 patients. In two patients renal calculi was present. One patient had increased renal cortical echoes, but she had normal renal function test and no proteinuria.

SUMMARY

1. Total number of cases enrolled were 20.
2. Incidence of Systemic sclerosis was 0.2 per 1000 dermatology cases.
3. The female to male ratio was 5.7:1.
4. 95% of cases were in the age group 21 -60 years
5. Youngest case was 10 years old and oldest was 53 years.
6. Occupational exposure to silica, solvents, pesticides and firework were present in 11 cases.
7. Mean duration of illness was 3.3 years.
8. Tightness of skin was seen in 100 % cases.
9. Skin tightness was the presenting complaint in 35% patients.
10. Hands, forearm, arm, face were involved in all cases. Lower limbs were less frequently involved.
11. Mean Modified Rodnan score was 18.
12. Difficulty in retracting the lower eyelid was present in all cases.
13. Pinched nose was seen in 70%
14. Fish mouth appearance and radial furrows around mouth was seen in 70% cases.
15. Difficulty in opening the mouth was present in 90 % cases.
16. All patients had sclerodactyly.

17. Raynaud's phenomenon was present in 65 %.

18. Fingertip ulcers were present in 60 % cases.

19. Stellate scars in the digits were present in 90%.

20. Round finger pad sign was seen in 85% cases.

21. All patients with Raynaud's phenomenon had Round finger pad sign.

22. 42% of patients without Raynaud's phenomenon had Round finger pad sign.

23. Two patients had gangrene and amputation of digits were done.

24. Pigmentary change was the second most common complaint

25. Salt and pepper pigmentation was present in 95% cases, most common site being retroauricular.

26. Generalized hyperpigmentation was seen in 45% cases.

27. Neck sign was seen in 80% cases.

28. One patient had calcinosis cutis.

29. Malar rash was present in one patient.

30. One patient had telengiectasia in both cheeks.

31. Loss of hair in the extremities was seen in 50% cases.

32. Hypohidrosis was seen in 65% cases.

33. One patient had leg ulcer.

34. Nail changes were present in 70% cases, most commonly ragged cuticles were present.

35. Other associated skin conditions reported were psoriasis, tinea versicolor, dermatophytosis, plantar wart.

36. Anaemia was present in 25% cases.

37. Elevate ESR was present in 70% patients.

38. Gastrointestinal, respiratory and musculoskeletal involvement were common.

39. Gastroesophageal refux was present in 85 % cases.

40. Endoscopy showed oesophagitis in 40% and lax gastroesophageal sphincter in 5%

41. Dysphagia was present in 40% cases.

42. Barium swallow studies showed dysmotility in 5% and narrowing of thoracic oesophagus in 5%.

43. Three patients had altered bowel habits, in one patient diarrhea was the presenting complaint.

44. Dyspnoea was present in 75% and dry cough in 35%

45. ILD was present in 95% cases.

46. Pulmonary function test showed restrictive pattern in 95%, of which it was mild in 20 % and moderate in 75%

47. One patient had pulmonary arterial hypertension.

48. Arthralgia was present in 45% cases.

49. One patient had overlap with Epidermolysis Bullosa Acquisita.

50. One patient had myositis, malar rash, arthralgia. U1RNP was positive and the diagnosis of MCTD was made.

51. X ray of hands showed acral osteolysis in 75% cases and osteopenia in 25% cases.

52. Acral osteolysis was present in 84.6% patients with Raynaud's phenomenon and 83.3% patients with fingertip scars.

53. No patient had renal involvement.

54. Hypothyroidism was present in two cases.

CONCLUSION

The incidence of Systemic sclerosis was 0.2 per dermatology cases. Female preponderance was present . It most commonly occurs from second to fourth decade, youngest patient being 10 years and the oldest being 53 years. Occupational exposure to harmful environmental factors like silica, solvents, pesticides, heavy metals in firework were present in more than half of the cases. Even though skin involvement was present in all cases, 20% of cases present only after systemic involvement. All the patients had diffuse involvement of skin. Only 65% patients had Raynaud's phenomenon, this is probably because of higher temperature present throughout the year in South India. 100 % of patients with Raynaud's phenomenon had Round finger pad sign. Round finger pad sign was also present in 42% patients without Raynaud's phenomenon. There was one case of overlap syndrome, who showed all features of Mixed Connective Tissue Disease. An interesting case of systemic sclerosis with Epidermolysis Bullosa Acquisita was reported. Systemic involvement was seen in most cases, mainly involving the pulmonary, gastrointestinal system. Interstitial lung disease was present in 95% cases. No patient had renal involvement. X ray of hands showed acral osteolysis and osteopenia and this correlated with Raynaud's phenomenon and fingertip scars.

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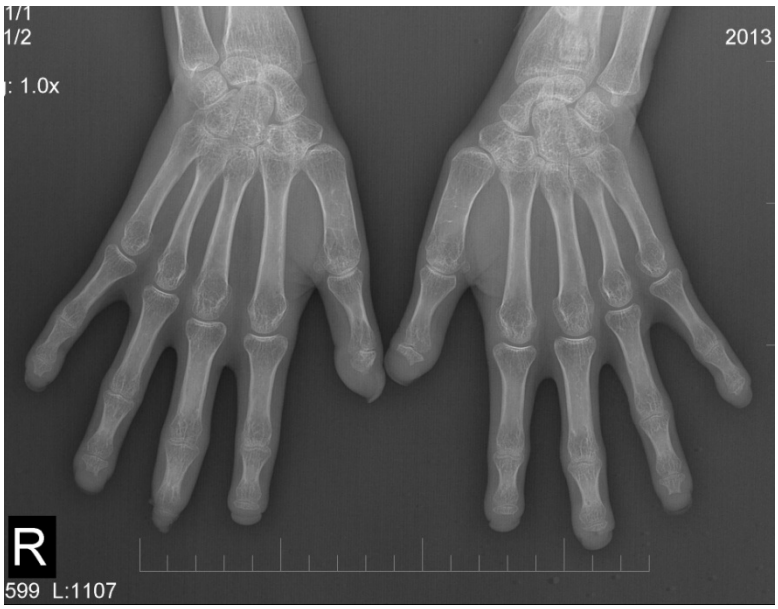
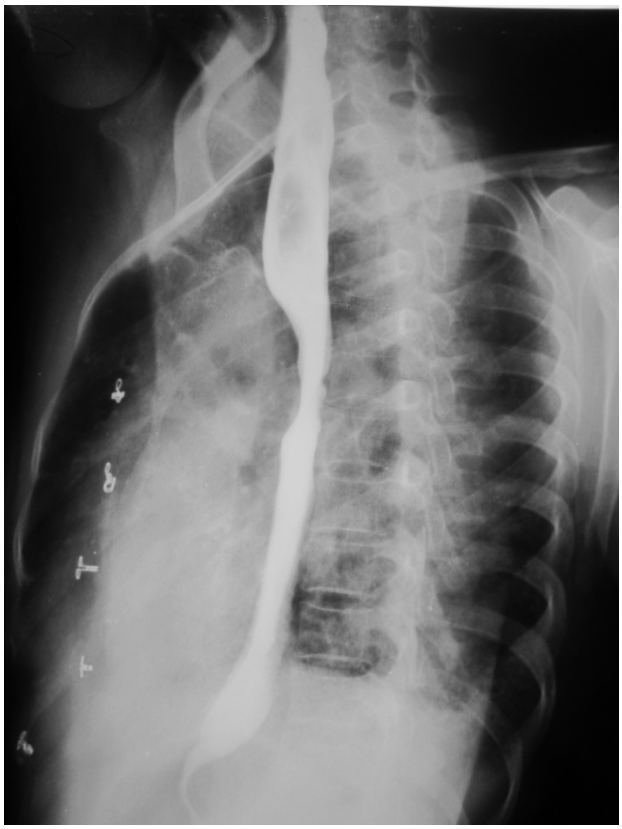
CLASSICAL SCLERODERMA FACIES – LOSS OF FOREHEAD WRINKLES, PINCHED NOSE, PURSED LIPS

MALE PATIENT WITH MINIMAL INVOLVEMENT

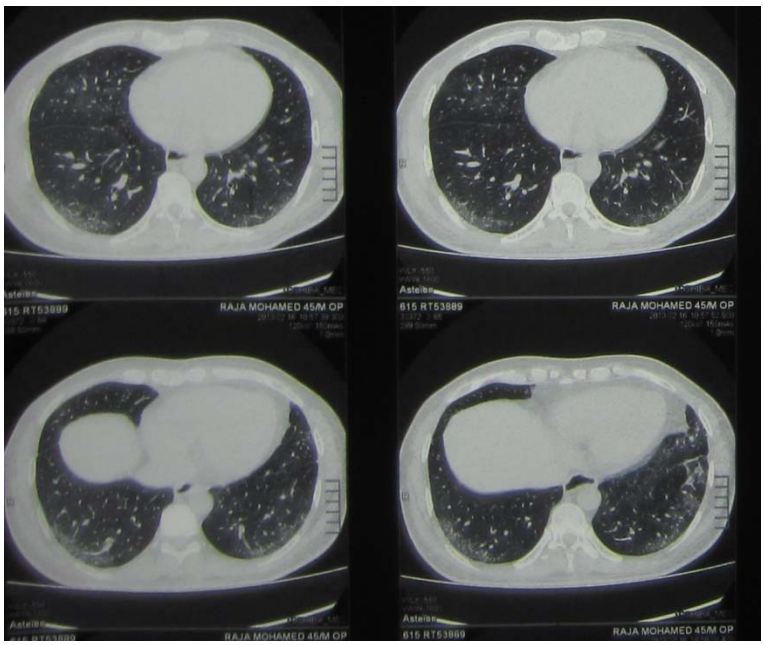
X RAY OF HANDS SHOWING ACRAL OSTEOLYSIS



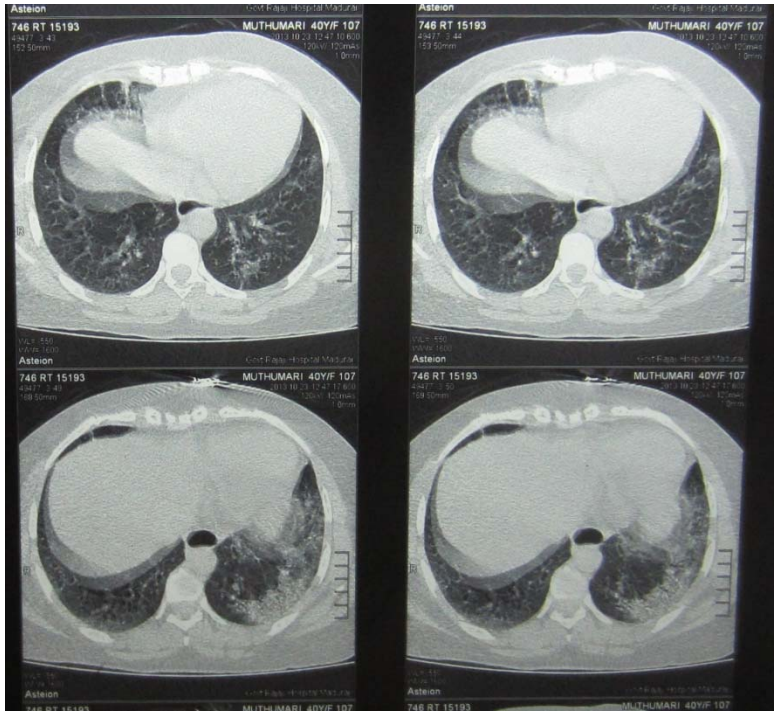
BARIUM SWALLOW SHOWING NARROWING OF THORACIC OESOPHAGUS



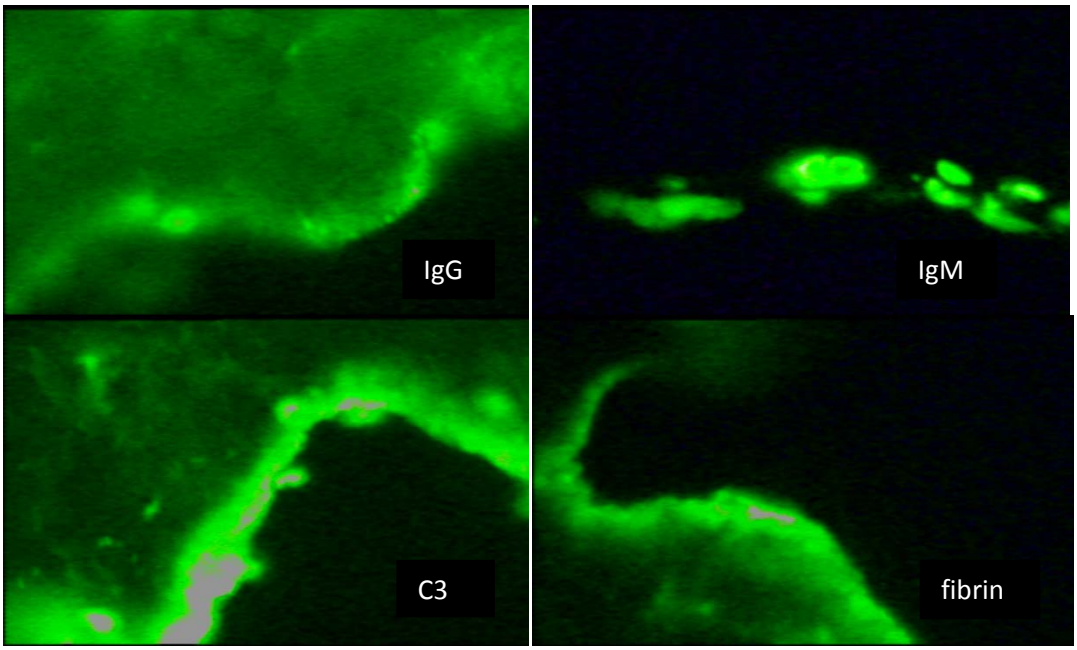
HRCT CHEST - INTERSTITIAL LUNG DISEASE



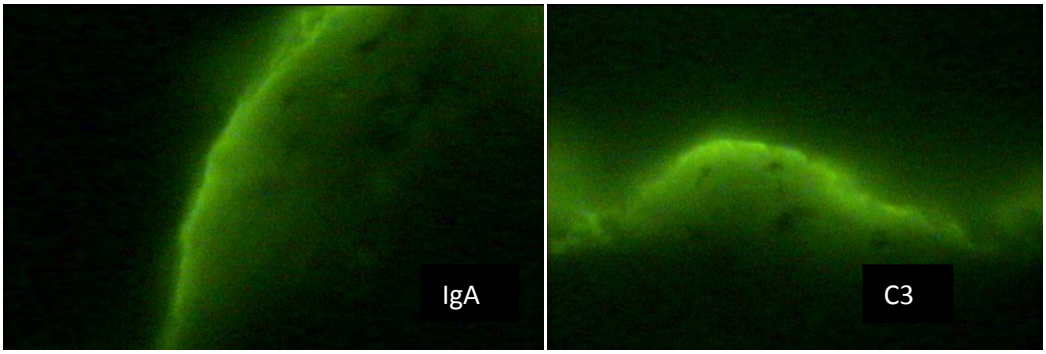
HRCT CHEST - INTERSTITIAL LUNG DISEASE



DIF – LINEAR AND GRANULAR DEPOSITS OF IgG,IgM,IgA, FIBRIN, C3 ALONG BASAL LAYER

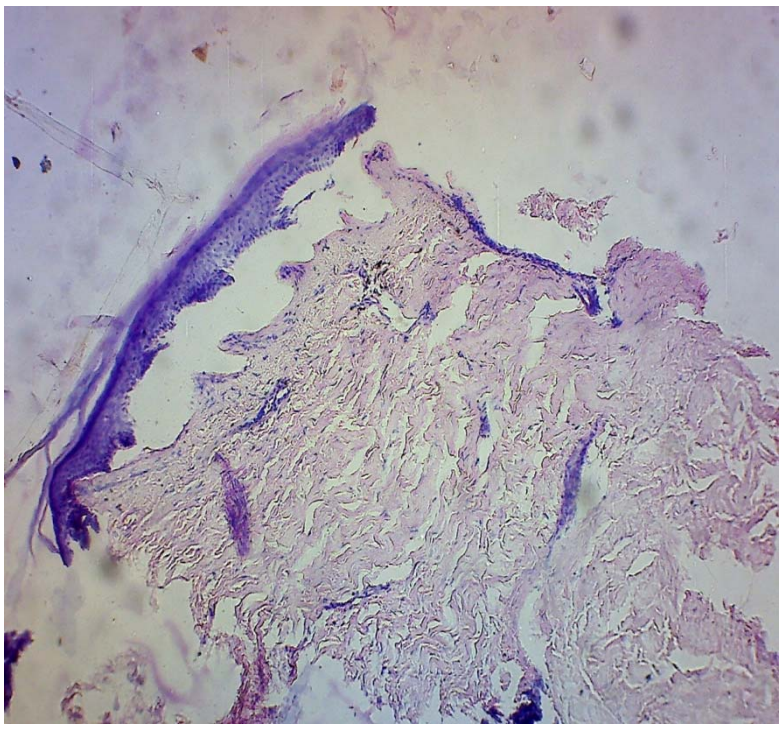


SALT SPLIT TECHNIQUE – LINEAR IgA AND C3 ALONG THE DERMAL SIDE



TENSE, LINEAR VESICLES AND BULLA WITH CLEAR FLUID AND EROSIONS IN THE BACKGROUND OF SCLERODERMATOUS SKIN OF EXTREMITIES

HISTOPATHOLOGY OF VESICLE SHOWING SUBEPIDERMAL BULLA WITHOUT INFILTRATE AND HYALINIZED COLLAGEN IN DERMIS



CALCINOSIS CUTIS

TELANGIECTASIA

CASE OF MIXED CONNECTIVE TISSUE DISEASE WITH MALAR RASH

LOSS OF LEFT INDEX FINGER

NAILS – RAGGED CUTICLES

RACQUET NAILS

EXTENSIVE SALT AND PEPPER PIGMENTATION

SALT AND PEPPER PIGMENTATION – CLASSICAL SITE – RETROAURICULAR AREA

SCLERODACTYLY WITH BEAKED NAILS

STELLATE FINGERTIP SCARS

SCLERODERMA FACIES – PINCHED NOSE, RADIAL FURROWS AROUND MOUTH

SCLERODACTYLY

PROFORMA

NAME:

AGE/ SEX:

OCCUPATION:

ADDRESS & PHONE NO:

HISTORY:

PRESENTING COMPLAINT – DURATION -

TIGHTNESS OF SKIN

DIFFICULTY IN MOUTH OPENING

RAYNAUD'S PHENOMENON

FINGERTIP ULCERS/ GANGRENE/ DIGIT LOSS

LEG ULCER

COUGH – TYPE

DYSPNOEA

CHEST PAIN

FATIGUE / MYALGIA / ARTHRALGIA

PROXIMAL MUSCLE WEAKNESS

DYSPHAGIA

RETROSTERNAL BURNING / REGURGITATION

BLOATING / CONSTIPATION / DIARRHOEA

ABDOMINAL PAIN / GI BLEED

PHOTOSENSITIVITY / RASH OVER FACE / ORAL EROSIONS / FEVER / SEIZURES

OTHERS

EXAMINATION:

ANEMIA / JAUNDICE / PEDAL EDEMA / LYMPH NODES

CVS-

RS- CREPTS, CHEST EXPANSION

P/A-

CNS-

BP- PULSE -

D/E:

HIDE BOUND SKIN – EXTENT – MODIFIED RODNAN SCORE

SCLERODACTYLY

PINCHED NOSE

FISH MOUTH/ RADIAL FURROWS

MACROGLOSSIA

DIFFICULTY IN MOUTH OPENING

DIFFICULTY IN RETRACTING LOWER EYELID

STELLATE SCARS / FINGER TIP ULCERS

DEMONSTRATION OF RAYNAUD'S PHENOMENON

ROUND FINGER PAD SIGN

NAILS – RAGGED CUTICLE / PTERYGIUM INVERSUM UNGUIS

CALCINOSIS CUTIS

SALT & PEPPER PIGMENTATION/ GENERALISED HYPERPIGMENTATION

NECK SIGN

LEG ULCER

ATROPHIE BLANCHE / LIVEDO RETICULARIS

LOSS OF HAIR / HYPO/ ANHYDROSIS

MUSCLE POWER / MUSCLE TENDERNESS

OTHERS

INVESTIGATIONS:

COMPLETE HEMOGRAM

URINE ROUTINE

RFT

LFT

CHEST X-RAY

PFT

HRCT

ECG

ECHO

USG – ABDOMEN & PELVIS

BARIUM SWALLOW

ENDOSCOPY

ANA, Scl 70

X- RAY – HANDS & FEET

OTHERS – EMG / MUSCLE BIOPSY / CPK/ SKIN BIOSY/DIF

MASTER CHART

	ip no	age	sex	age of onset	occupation	exposure	presenting complaint	duration of illness	tightness of skin	fingertip ulcer	gangrene	cough - type	dyspnoea	chest pain	myalgia	arthralgia	proximal muscle weakness	dysphagia	retrosternal burning	altered bowel habits	abdominal pain / GI bleed	others	General conidition	RS - crepts	chest expansion in cm	extent of involvement	modified Rodnan score	sclerodactyly	pinched nose	radial furrow/ fish mouth	difficulty in mouth opening	retraction of lower eyelid	stellate scars	digit loss	raynaud's phenomenon	round finger pad sign	nails	calcinosis cutis	generalised pigmentation	salt & pepper pigmentaion	neck sign	leg ulcer	loss of hair	hypohydrosis	muscle tenderness	others	Complete blood count	ESR	Renal function test	Liver function test	chest X ray	HRCT chest	Pulmonary function test	ECG	ECHO	USG abdomen and pelvis	Barium swallow	endoscopy	Xray -hands n feet	others
1	23236	40	F	36	packing	n	f u	4	p	p	n	n	n	p	n	n	n	p	p	n	n	n	N	n	3	fi,h,fa,a,f	14	p	p	n	p	p	n	n	p	p	rq	n	p	ra	p	n	p	p	n	t.v.	N	20	N	N	ILD	ILD	mod	N	N	N	N	N	ao	N
2	34212	29	F	27	tailor,packing	n	ar	2	p	p	n	n	p	n	p	p	n	p	p	n	n	n	an	n	3	fi,h,fa,a,f,c	18	p	p	p	p	p	p	n	p	p	n	p	p	ra,s,fa	p	n	p	p	n	t.c.	Hb-9.8	46	N	N	N	ILD	mod	N	N	N	N	N	ao,o	N
3	24532	59	F	52	housewife	n	GERD	7	p	n	n	n	p	n	n	n	n	p	p	p	n	n	N	n	3	fi,h,fa,a,f	14	p	n	p	p	p	n	n	p	n	r c	n	p	ra,f, fa, l	p	n	n	n	n	n	N	55	N	N	N	ILD	mod	N	N	N	N	E	N	hypothyroidism
4	23476	23	F	23	firework	4y	p c	1	P	n	n	n	n	n	n	n	n	n	n	n	n	n	N	n	2	fi,h,fa,a,f	20	p	n	n	p	p	p	n	n	p	r c	n	p	ra,f	n	n	n	p	n	n	N	60	N	N	ILD	ILD	mild	N	N	N	N	N	ao	N
5	25431	25	F	23	match box	10y	f u	2	p	p	p	n	p	n	n	p	n	n	p	n	n	n	N	n	2	fi,h,fa,a,f,c,ab	23	p	p	p	p	p	p	n	p	p	r c	n	p	ra	p	n	n	n	n	n	N	5	N	N	ILD	ILD	mod	N	N	N	N	N	ao,o	N
6	26523	45	M	44	stone cutter	30 y - sil	dysp	1	p	n	n	p-d	p	n	n	p	n	n	p	n	n	n	N	p	2	fi,h,fa,a,f	14	p	p	n	n	p	p	n	p	p	lm	n	p	n	p	n	n	n	n	psoriasis	N	90	N	N	ILD	ILD	mod	N	N	N	N	E	ao	N
7	23789	55	F	53	Al polishing	25y - sol	p c	2	p	p	n	p-d	p	n	p	p	n	p	p	n	n	n	N	n	3	fi,h,fa,a,f,c,ab	18	p	n	p	p	p	p	n	n	p	r c	n	n	fa	p	n	p	p	n	n	N	65	N	N	ILD	ILD	mod	N	N	N	N	N	ao	hypothyroidism
8	26141	35	F	27	agriculture	10y- pes	s t	8	p	p	p	p-d	p	n	p	n	n	p	p	n	n	n	an	n	2	fi,h,fa,a,f,l,c,ab	28	p	p	p	p	p	p	LMF	p	p	r c	n	n	ra,s, fa,l	p	n	p	p	n	n	Hb-6.2	10	N	N	ILD	ILD	mod	lwc	N	N	D	E	ao,o	N
9	20993	45	M	42	cleaning	10y- sol	s t	3	p	p	n	n	p	n	p	p	n	n	p	n	n	n	N	n	3	fi,h,fa,a,f	16	p	n	n	p	p	p	L,R IF	n	p	rq	n	n	ra, fa,l	p	n	n	p	n	n	N	5	N	N	ILD	ILD	mod	N	N	RC	N	N	ao,o	N
10	28832	38	F	33	firework	15 y	f u	5	p	p	n	n	n	n	n	n	n	n	p	n	n	n	N	n	4	fi,h,fa,a,f	14	p	p	p	p	p	p	n	p	p	n	n	n	ra	p	n	p	p	n	n	N	75	N	N	N	ILD	mod	N	N	RC	N	E	N	N
11	31445	48	F	45	housewife	n	R	3	p	n	n	n	p	n	p	p	p	n	p	n	n	malar rash	N	n	2	fi,h,fa,a,f,c	16	p	p	p	p	p	p	n	p	p	r c	n	p	ra	p	p	p	p	p	LE,DM	N	80	N	N	N	ILD	mod	N	N	N	N	N	ao	U1 RNP
12	28542	50	F	45	agriculture	30y	s t	5	p	n	n	p-d	p	p	p	p	n	n	p	p	n	blisters	an	p	2	fi,h,fa,a,f,c,l,t,fe	37	p	p	p	p	p	p	n	p	p	r c	n	p	l,t,h	p	n	p	p	n	bulla	Hb-9	45	N	N	ILD	ILD	mod	N	PAH	N	N	N	ao	ANA + scl70 + ds DNA -
13	27604	29	M	28	office assistant	n	s t	1	p	n	n	n	p	n	n	n	n	n	p	n	n	n	N	n	3	fi,h,fa,a,f,c	14	p	p	n	n	p	n	n	n	n	n	n	n	ra	n	n	n	n	n	n	N	30	N	N	N	ILD	mild	N	N	N	N	N	N	N
14	32987	42	F	39	Iron polishing	10 y - sol	s t	3	P	p	n	p-d	p	p	p	n	n	p	p	n	n	n	N	p	2	fi,h,fa,a,f	14	p	p	p	p	p	p	n	p	p	r c	n	n	ra	p	n	p	p	n	n	N	165	N	N	ILD	ILD	mod	N	N	irce	NE	E	ao,o	N
15	27798	45	F	44	agriculture	20y - pes	s t	1	p	n	n	n	n	n	n	n	n	n	n	n	n	n	N	p	2	fi,h,fa,a,f,l	16	p	n	p	p	p	p	n	n	p	r c	n	p	ra,fa,f,c	p	n	p	p	n	n	N	20	N	N	ILD	ILD	mod	N	N	N	N	E	ao	N
16	20687	17	F	10	student	n	p c	7	p	p	n	p-d	p	n	p	p	p	p	p	n	n	n	N	p	3	fi,h,fa,a,f,c,ab,l	30	p	p	p	p	p	p	n	p	p	r c	n	n	ra, fa,f	p	p	p	p	n	n	N	70	N	N	ILD	ILD	mod	N	N	N	N	E	ao	N
17	24456	53	F	49	housewife	n	diar	4	p	p	n	n	p	n	n	n	p	p	p	p	n	n	N	n	3	fi,h,fa,a,f	13	p	p	p	p	p	p	n	p	p	n	n	n	ra, fa	p	n	n	p	n	n	N	35	N	N	N	ILD	mild	N	N	N	N	E	ao	N
18	26732	41	F	36	housewife	n	R	5	p	p	n	p-d	p	n	p	p	p	n	p	n	n	n	an	p	2	fi,h,fa,a,f,fe	14	p	p	p	p	p	p	n	p	p	r c	p	n	-	n	n	n	n	n	telangiec	Hb- 9	65	N	N	ILD	ILD	mod	N	N	N	N	N	N	N
19	25683	35	F	32	housewife	n	p c	3	p	p	n	n	p	n	n	n	n	n	p	n	n	n	N	n	3	fi,h,fa,a,f,l	18	p	p	p	p	p	p	n	p	p	r c	n	n	ra,fa	p	n	n	n	n	n	N	45	N	N	N	ILD	mild	N	N	N	N	Lax E	ao	N
20	24567	28	F	27	agriculture	15y-pes	s t	1	P	n	n	n	n	n	n	n	n	n	n	n	n	n	an	n	4	fi,h,fa,a,f	14	p	n	n	p	p	p	n	n	n	n	n	n	ra	n	n	n	n	n	wart	Hb- 7.4	55	N	N	N	N	N	N	N	N	N	N	N	N

KEY TO MASTER CHART

a – Arm

ab – abdomen

Al polishing – Aluminium polishing

an – anaemia

ao – acral osteolysis

ar – arthralgia

c – chest

D – Dysmotility

DM – dermatomyositis

dysp – dyspnoea

E – esophagitis

f – face

F – female

f u – fingertip ulcer

fa – forearm

fe – feet

fi - finger

GERD – gastro esophageal reflux disease

h – hand

Hb – hemoglobin

ILD – interstitial lung disease

irce – increased renal cortical echoes

l – leg

L, RIF – left, right index finger

Lax E – lax gastroesophageal sphincter

LE – lupus erythematosus

lm – longitudinal melanonychia

LMF – left middle finger

lwc – low voltage QRS complex

M – male

mod – moderate

N – normal

n – not present

NE – narrowing of thoracic oesophagus

o – osteopenia

p – present

p c – pigment change

PAH – pulmonary arterial hypertension

p-d – present, dry type

pes – pesticides

R – Raynaud's phenomenon

ra – retroauricular

rc – ragged cuticles

RC – renal calculi

rq – racquet nails

s – scalp

s t – skin tightness

sil	–	silica
sol	–	solvents
t	–	thigh
t.c.	–	tinea corporis
t.v.	–	tinea versicolor
telangiec	–	telangiectasia
y	–	years

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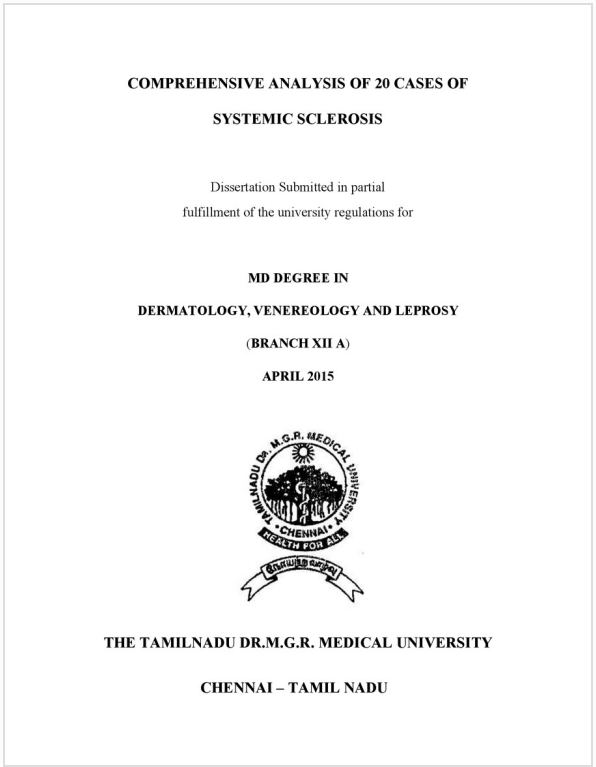

COMPREHENSIVE ANALYSIS OF 20 CASES OF

SYSTEMIC SCLEROSIS

Dissertation Submitted in partial
fulfillment of the university regulations for

MD DEGREE IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

(BRANCH XII A)

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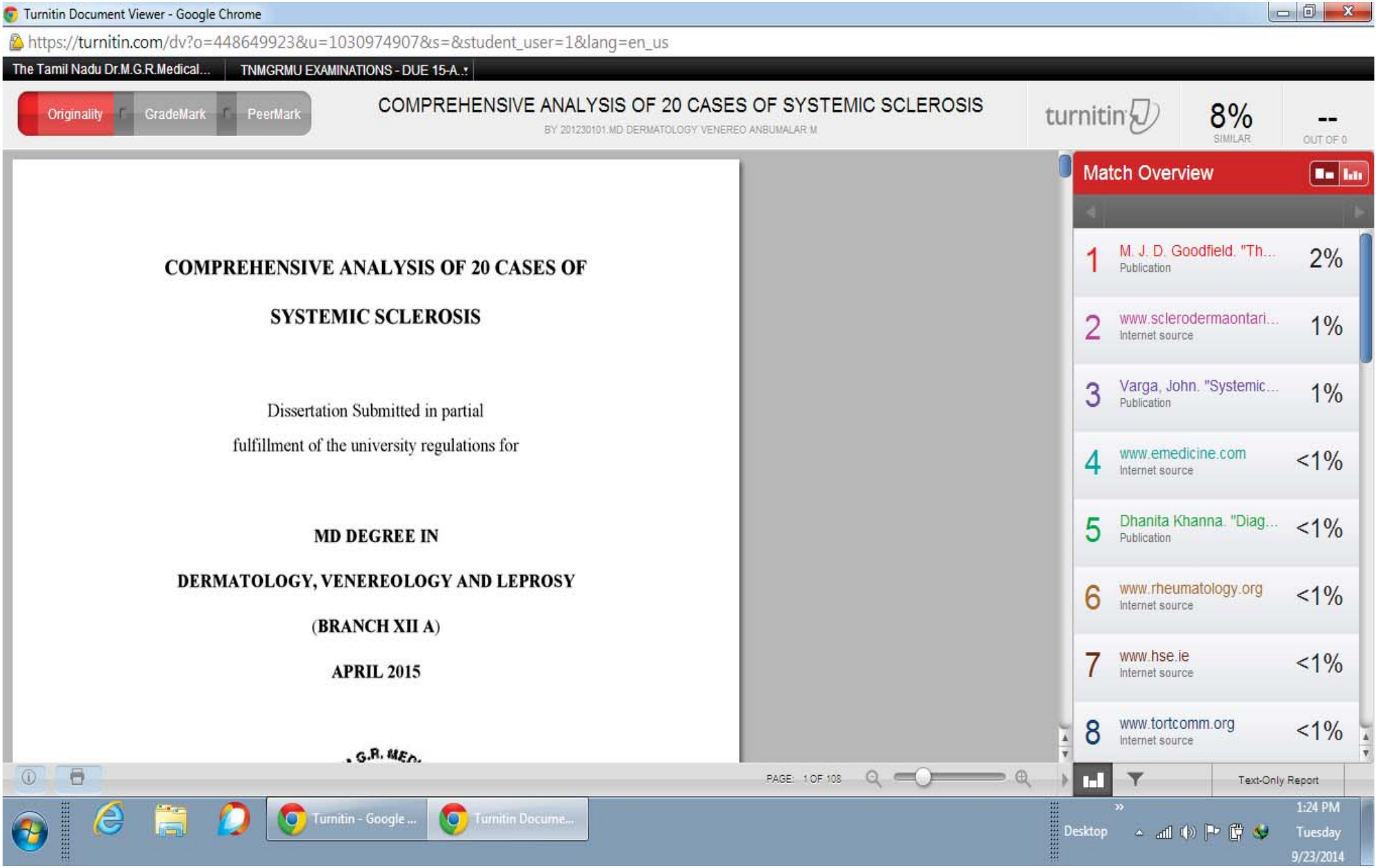
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Institutional Review Board / Independent Ethics Committee.
Capt. Dr.B. Santhakumar, M.D., (F.M.,) deanmdu@gmail.com
Dean, Madurai Medical College &
Govt Rajaji Hospital, Madurai 625020. **Convenor**

Sub: Establishment-Govt. Rajaji Hospital, Madurai-20-
Ethics committee-Meeting Minutes- for February 2014
Approved list - Regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held on 07.02.2014, Friday at 10.00 am to 12.00.noon at the Anaesthesia Seminar Hall, Govt. Rajaji Hospital, Madurai. The following members of the committee have attended the meeting.

1.Dr.V. Nagarajan, M.D., D.M (Neuro) Ph: 0452-2629629 Cell.No 9843052029 nag9999@gmail.com	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2. Dr.Mohan Prasad , M.S M.Ch Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology(Retired) D.No.32, West Avani Moola Street, Madurai -1	Member Secretary
3. Dr. Parameswari M.D (Pharmacology) Cell.No.9994026056 drparameswari@yahoo.com	Director of Pharmacology Madurai Medical College	Member
4. Dr.S. Vadivel Murugan, MD., (Gen.Medicine) Cell.No 9566543048 svadivelmurugan_2007@rediffmail.com	Professor& H.O.D of Medicine Madurai Medical College	Member
5. Dr.S. Meenakshi Sundaram, MS (Gen.Surgery) Cell.No 9842138031 drsundarms@gmail.com	Professor & H.O.D of Surgery Madurai Medical College	Member
6. Mrs. Mercy Immaculate Rubalatha, M.A., Med., Cell. No. 9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's quarters, Gandhi Museum Road, Thamukam, Madurai-20	Member
7. Thiru..Pala. .Ramasamy , BA.,B.L., Cell.No 9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72.Palam Station Road, Sellur, Madurai -2	Member
8. Thiru. P.K.M. Chelliah ,B.A Cell.No 9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20	Member

The following Projects was approved by the committee.

Name of P.G.	Course	Name of the Project	Remarks
Dr. M. Anbumalar dr.anbumalar.cmc@gmail.com	PG in M.D., (DVL), Government Rajaji hospital, Madurai Medical College, Madurai.	Comprehensive analysis of 20 cases of systemic sclerosis	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.

2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.

3. She/He should not deviate the area of the work for which applied for Ethical clearance.

She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.

4. She/He should abide to the rules and regulations of the institution.

5. She/He should complete the work within the specific period and if any

Extension of time is required He/She should apply for permission again and do the work.

6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.

7. She/He should not claim any funds from the institution while doing the work or on completion.

8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Member Secretary **Chairman**
Ethical Committee

DEAN/Convenor 26.2.14
Govt. Rajaji Hospital,
Madurai- 20.

24/2/14

To
The above Applicant
-thro. Head of the Department concerned